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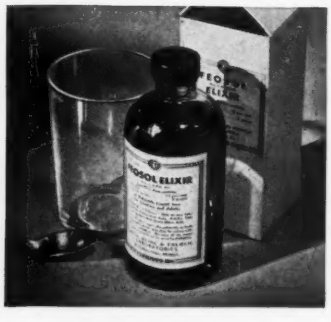

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1 Archiv. of Path., Feb. 1929.
2 Soc. Exp. Biol. & Med., May 1929.
3 Soc. Exp. Biol. & Med., 45-361, 1940.

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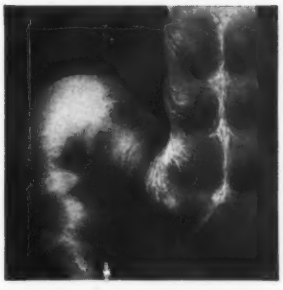

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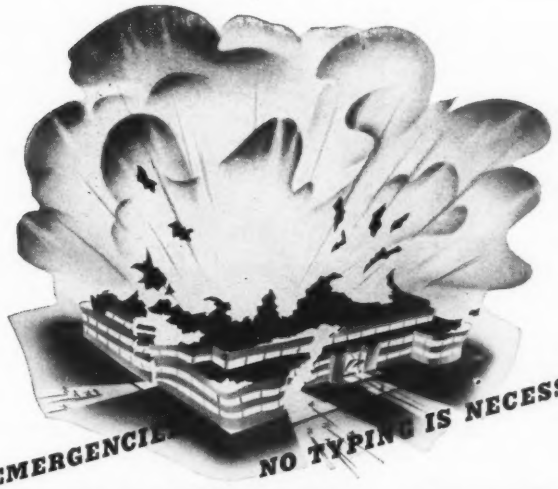

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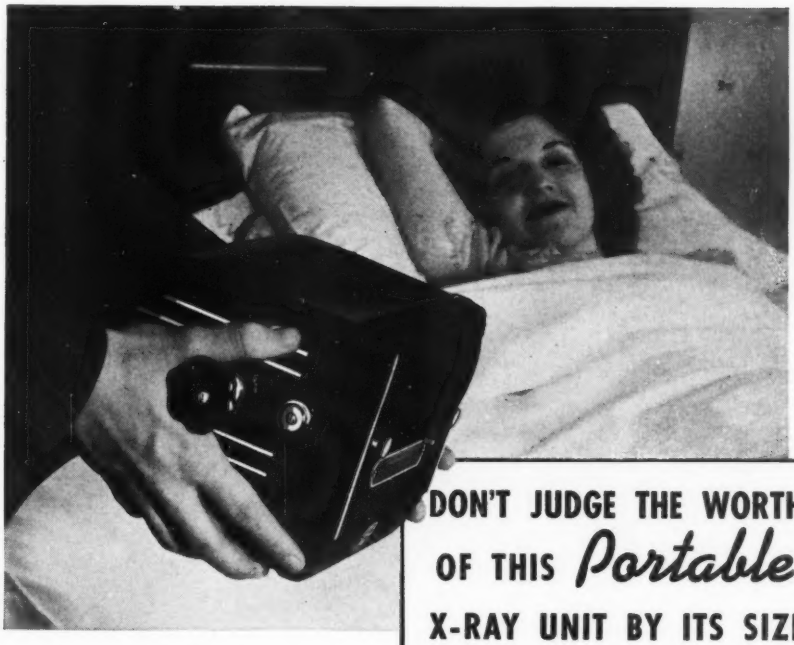

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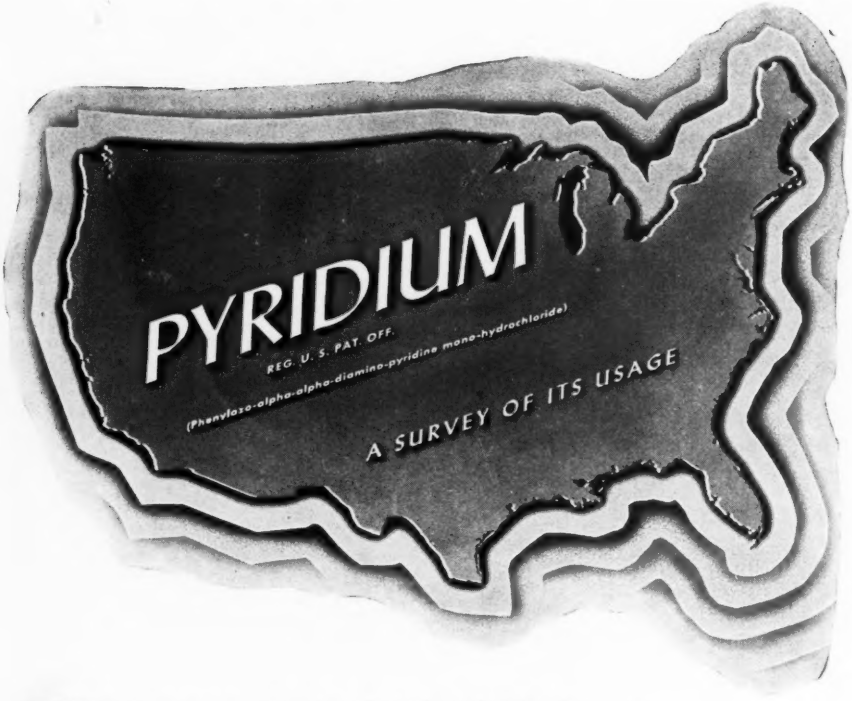

THE response to a questionnaire submitted to physicians in various areas of the country shows that the principal urogenital conditions in which Pyridium has been found effective are, cystitis, pyelitis (pyelonephritis), urethritis, and prostatitis in the order given. This closely approximates the experiences of those who have contributed to the published literature.

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PYRIDIUM is the United States Registered Trade-Mark of the product manufactured by Pyridium Corporation.

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TRADE MARK
(Phenyluza-Alpha-Alpha-Diamino-Pyridine Mono-Hydrochloride)
A decade of service in urogenital infections

MERCK & CO. Inc. *Manufacturing Chemists* RAHWAY, N. J.

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'Delvinal' Sodium

A Sedative and Hypnotic of Superior Clinical Merit

Extensive investigation has shown that 'Delvinal' Sodium [Sodium 5-ethyl 5-(1-methyl 1-butenyl) barbiturate], in comparison with other barbiturates, is characterized by:

- *Safe therapeutic index*
- *Moderate duration of action*
- *Rarity of "drugged" sensation during induction period*
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- *Relative freedom from "hangover"*

'DELVINAL' SODIUM is indicated for use as a general sedative and hypnotic and in the relief of insomnia and excited mental states. It is of especial value in the production of preoperative sedation, preanesthetic hypnosis, and obstetrical sedation and amnesia.

'Delvinal' Sodium is supplied in dry-filled colored gelatin capsules in two strengths: ½ grain (brown) in bottles of 100, 500 and 1000; 1½ grain (light orange) in bottles of 25, 100, 500 and 1000.

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The administration of nicotinic acid in appropriate doses in cases of pellagra leads to the clearing of alimentary lesions and symptoms, including the typical glossitis, to the disappearance of dermal lesions characteristic of the disease, and to profound improvement in the mental symptoms when the latter are the result of inadequate intake of nicotinic acid.

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Nicotinic acid is pyridine-3-carboxylic acid—$C_6H_5O_2N$. It is recognized as a specific in the treatment of the disease of dogs known as blacktongue and in the treatment of human pellagra.

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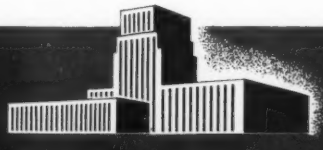

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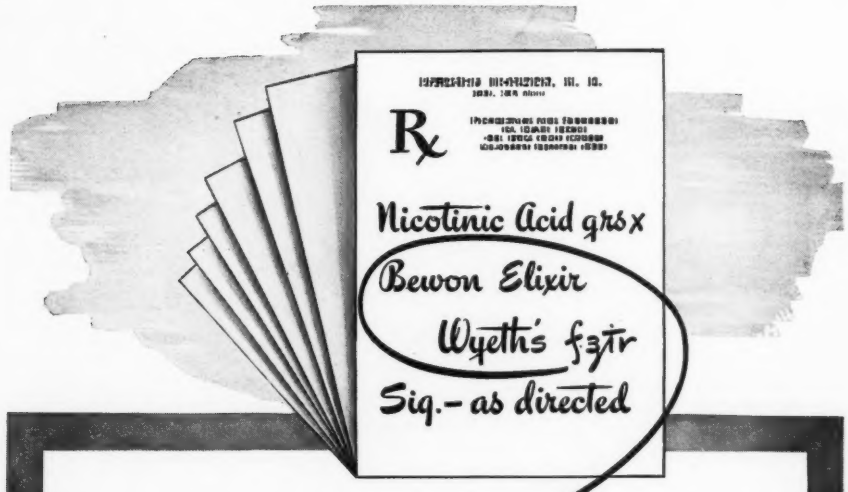

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Bewon Elixir is compatible with most drugs, contains 19% alcohol and is slightly acid in reaction.

Standardized to contain 500 International Units of Vitamin B_1 (thiamin chloride) Bewon Elixir stimulates the appetite and is indicated in Vitamin B_1 deficiencies.

Supplied in pint and gallon bottles

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ACCEPTED AMERICAN MEDICAL ASSN.

Made from fresh skim milk (casein modified) with added lactose, salts, milk fat, and vegetable and codliver oils.

In human milk 2/3 of the protein is in true solution, while in cow's milk only 1/6 of the protein is soluble. During the process employed in preparing Similac the soluble proteins in cow's milk are increased to a point approximating the soluble proteins in human milk. How greatly this improves the digestibility is indicated by a comparison of the curd (insoluble calcium paracaseinate) formed by cow's milk, with the soft flocculent curd of Similac. The softer the curd the shorter the digestive period.* Similac, like breast milk, has a consistently zero curd tension.

* Espe & Dye—"Effect of Curd Tension on the Digestibility of milk"—Amer. Journal Diseases of Children—1932, Vol. 43, p. 62.

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Continuous Mild Sedation Without Depression

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Indications: Cardiac, gastric, and other functional disorders; and wherever else continuous mild sedation is desired.

SOLFOTON is also available with 1/200 grain Atropine Sulfate in each tablet under the name of ANTROCOL.

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EACH TABLET CONTAINS
Phenobarbital . . . . gr. ¼
Sulfur . . . . . gr. ⅓

The colloidal character of the sulfur in SOLFOTON is produced under the protection of U. S. Patent 1,934,989.

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Since 1856

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ARTHRITIC
PATIENT WITH

RELIEF FROM PAIN

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(ACETYL-BETA-METHYLCHOLINE CHLORIDE OINTMENT)

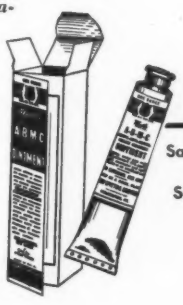
A-B-M-C Ointment relieves arthritic pain because of its local action in increasing the blood supply to the affected part by dilatation of the arterioles and capillaries.

In 88 percent of 96 patients studied, A-B-M-C Ointment provided relief from pain without any untoward effects when used as directed. No urticaria was produced in any case.†

A-B-M-C Ointment is spread, without rubbing, on the affected part and heat is applied for 20 minutes.

†Archives of Physical Therapy, *21*, 12 (Jan.) 1940.

**A-B-M-C Ointment is a trademark of John Wyeth & Brother, Incorporated, for its brand of ointment containing Acetyl-Beta-Methylcholine Chloride 0.25%, thymol, eucalyptol and methyl salicylate in an emollient base.*



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The Tucker Sanatorium is for the treatment of nervous and endocrine diseases. There are departments of massage, medicinal exercises, hydrotherapy and physiotherapy. The Sanatorium is large and bright, surrounded by a lawn and shady walks, large verandas and has a roof garden. It is situated in the best part of Richmond and is thoroughly and modernly equipped. The nurses are specially trained in the care of nervous cases.

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The School of Nursing is affiliated with Johns Hopkins Hospital School of Nursing in Baltimore for a three months' course each in Pediatrics and Obstetrics.

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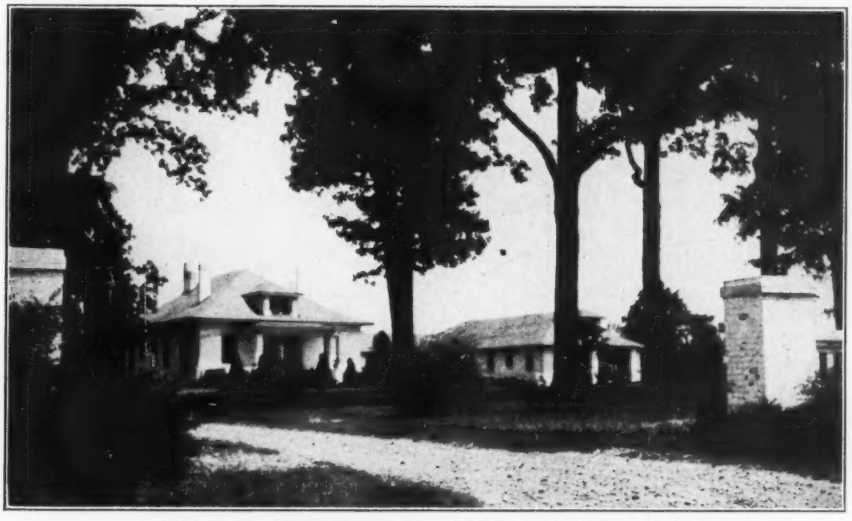

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For the Diagnosis and Treatment of Mental and Nervous Disorders

Located on the Raleigh-La Grange Road, five miles east of the city limits. Accessible to U.S. 70 (the Bristol Highway). 53½ acres of wooded land and rolling fields. Equipment new and modern, including the latest equipment for physical and hydrotherapy. Special emphasis is laid upon occupational and recreational therapy under the supervision of a trained therapist. An adequate nursing personnel gives individual attention to each patient.

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Admits patients irrespective of denomination or creed.

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New, distinctive, Individual **Bungalows,** highly modern, and **Private Rooms** with baths and sleeping porches, all equipped with radio.—Beautiful grounds.

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Established 1890 **MILLEDGEVILLE, GA.**
For the treatment of

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Grounds 600 Acres — Buildings Brick, Fireproof — Comfortable — Convenient — Site High and Healthful
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Diagnosis and Treatment of Nervous and Mental Diseases, Alcoholic and Drug Addictions. Especially equipped for the Treatment of Mental Disorders. Convalescents, Elderly People and those requiring METRAZOL THERAPY given special monthly rates. Personal supervision of patients. Consulting physicians.

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Approved diagnostic and therapeutic methods. Hydrotherapy, Electrotherapy, Massage, X-Ray and Laboratory.

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Appalachian Hall is located in Asheville, North Carolina. Asheville justly claims an unexcelled all year round climate for health and comfort. All natural curative agents are used, such as physiotherapy, occupational therapy, outdoor sports, horseback riding, etc. Five beautiful golf courses are available to patients. Ample facilities for classification of patients. Rooms single or en suite with every comfort and convenience.

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Richmond, Virginia

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The institution is situated just beyond the northern border of the city on United States Highway Number 1.

The scope of the work of the Sanatorium is limited to the diagnosis and the treatment of nervous and mental disorders and to the addictions to drugs and to alcohol. It affords also adequate facilities for rest and upbuilding under medical and nursing supervision.

The medical staff devotes its entire attention to the patients in the Sanatorium.

The institution maintains a school for trained attendants in which instruction in the care of the nervous and mentally sick is emphasized.

There are twelve separate buildings for patients with 150 beds. Such a large group of buildings makes possible the more congenial grouping of patients. Rooms may be had single or en suite, with or without private bath. There are a few small cottages for the use of individual patients.

A comprehensive general physical and nervous examination is made of each patient. A mental examination is made when indicated. The examination is typed and a copy of it is available for the referring physician. Complete dental investigation is a part of the general survey.

A skilled teacher gives practical daily instruction to small groups in the arts and crafts. Helpful and interesting occupation in the out-of-doors is made possible for the men patients in the vegetable and flower gardens, on the truck farm, in the poultry yards, and in the dairy.

There are bowling, tennis, croquet and pool. On Sunday evening there is chapel service.

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AN ENTIRELY NEW PLANT ERECTED IN 1922

Separate buildings for men and women, ideally arranged and equipped with every facility for the comfort, care, and treatment of the class of patients received.

It is upon the character of service rendered, rather than upon physical facilities that the reputation of such an institution must rest, and to give every patient the maximum of individual attention and unremitting care at all times is the basic principle of our work. An efficient organization exists in all departments. There is maintained an abundantly sufficient staff of capable nurses, divided into day and night shifts, assuring to every patient constant service through each of the twenty-four hours of the day. At midnight this service is as real as at midday.

Situated in the midst of a fifty-acre tract and surrounded by a large grove and attractive lawns.

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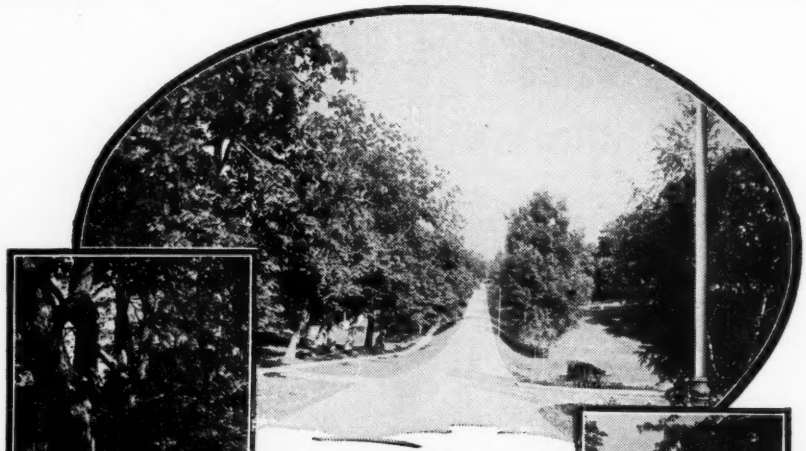
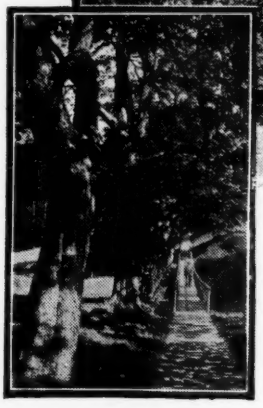
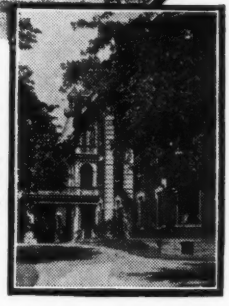
Reference: The Medical Profession of Nashville







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A strictly modern hospital fully equipped for the scientific treatment of nervous and mental affections. Situation retired and accessible. For details write for descriptive pamphlet.

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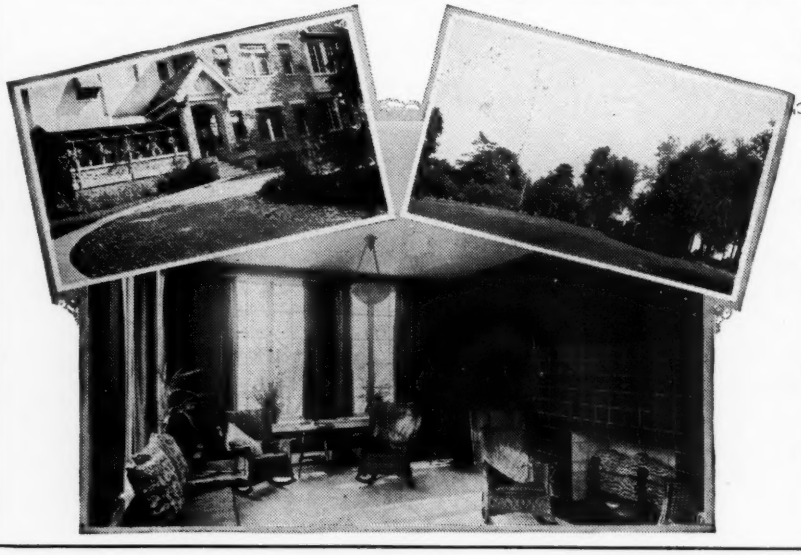

For purely nervous cases, nutritional errors and convalescents.

Completely equipped for hydrotherapy, massages, etc.

Cuisine to meet individual needs.

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Thoroughly modern in architecture and construction. Eight departments—affording proper classification of patients. All outside rooms attractively furnished. Several bathrooms and rooms with private bath on each floor. Also a spacious sun parlor in each department. Located on the crest of Higdon Hill, 1050 feet above sea level, overlooking the city, and surrounded by an expanse of beautiful woodland. Ample provision made for diversion and helpful occupation. Adequate night and day nursing service maintained.

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References: Medical profession of Birmingham and Birmingham Chamber of Commerce.

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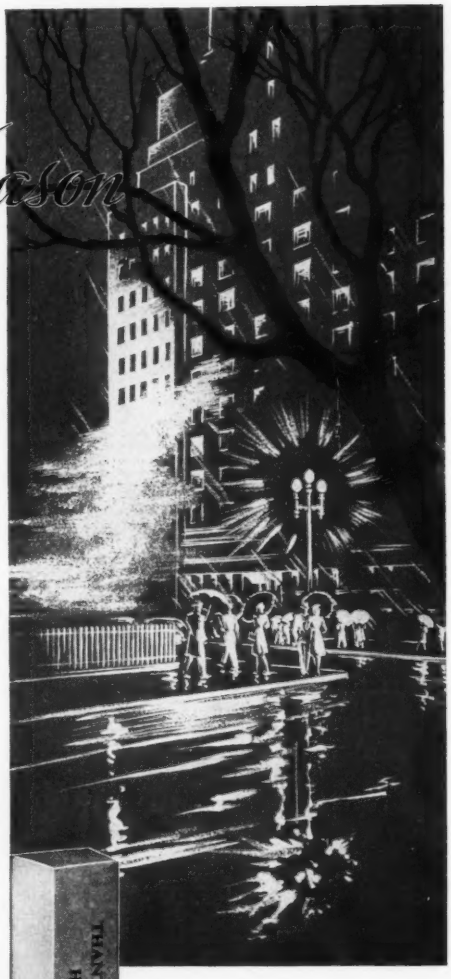
For over thirty years in successful operation; just eight miles from the heart of the city, in a quiet suburb, occupying sixteen acres of beautiful grounds, this Sanitarium is especially equipped for the treatment of drug addiction, alcoholism, nervous, and mental disorders, the care of patients requiring metrazol and insulin therapy and is ideal for convalescents.

Thantis Season



Wintry weather brings with it the usual prevalence of throat affections.

Thantis Lozenges, H. W. & D., were developed for medical use in the treatment of throat soreness and irritation and following tonsillectomy. They dissolve slowly, permitting prolonged throat medication.

Thantis Lozenges, H.W.&D. are convenient and economical. They are antiseptic and anesthetic for the mucous membranes of the throat and mouth.

Thantis Lozenges contain Merodicein, H. W. & D., 1/8 grain, and Saligenin, H. W. & D., 1 grain.

THANTIS LOZENGES *are supplied in vials of twelve lozenges each.*

HYNSON, WESTCOTT & DUNNING, INC.

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1941

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TREATMENT OF LARYNGEAL PAPILLOMA IN CHILDREN*

By EDWIN N. BROYLES, M.D.
Baltimore, Maryland

When a child is brought into the office with a complaint of long standing hoarseness, it is with some feeling of dread that we go about the diagnosis.

Occasionally in small children, the larynx can be examined satisfactorily with a mirror, but in the great majority of cases, a direct laryngoscopy is required for the determination of the cause of hoarseness. If with a mirror or with a direct laryngoscope, the larynx is seen to be covered with small wart-like tumors, and the microscopic section looks like *Fig. 1*, the diagnosis is papilloma of the larynx.

This is a common benign tumor of the larynx in children, and may lead to dreaded complications. So far as I know, the etiology of papilloma is unknown, although Ullman[1] of Vienna transplanted the growth by a filterable virus.

Papillomata also occur in adults. But although the microscopical picture is identical (*Fig. 2*), the behavior of papilloma of adults and children is entirely different.

A papilloma of the larynx in adults when completely removed, does not recur and does not spread, whereas papillomata of the larynx in children tend to multiply and to implant themselves on the mucous membrane of the larynx, epiglottis, trachea or even of the mouth and lips. No wonder, then, that there is some dread in the recognition of the possibilities of this disease. Papilloma of the larynx in children has another strange characteristic. Suddenly the growths may stop multiplying, the spreading and implanting characteristic stops, and they can be removed with no recurrence. This usually takes place around or during puberty. The fact that treatment is not satisfactory is shown by the number of remedies suggested. X-ray, radium, laryngofissure and frequent removal have been tried and if the larynx is not kept comparatively clear, the patient may die from asphyxia due to filling up of the trachea or larynx. For this reason, the one point in common of all the treatments has been an early tracheotomy.

Semon[2] mentions a case in which no fewer than 17 thyrotomies had been performed on the same patient with recurrence of the growth on each occasion.

Robinson has recorded a case in which endolaryngeal operations had been performed 19 times, tracheotomy 3 times, intubation 3 times, thyrotomy and laryngotomy. Death took place suddenly and at postmortem it was found that papillomata filled the larynx.

According to Holt, [3 4] operative removal of these papillomata usually results in their recurrence in increased numbers. For this reason operations through the mouth have been largely given up. A tracheal tube must be worn from six months to a year.

Thompson also mentions the necessity of frequent removal and of the patients wearing a tube for 2 or more years.

Ballenger[5] discusses early tracheotomy and frequent removals.

B. V. Burns reports 127 cases of children with papillomata: 48 were not operated upon; 32 died, 28 by suffocation; 3 were cured spontaneously; 26 had tracheotomy of whom 7 died (25 per cent mortality); 21 had laryngofissure with 8 cured; 40 had intralaryngeal operations with 13 cures.

Rosenberg reported 109 cases that had laryngofissure; 20 patients died from suffocation due to recurrence. In 43 cases there was recurrence

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*From the Department of Laryngology, Johns Hopkins Hospital.

after repeated operations, although 40 were cured.

When growths show a stage of quiescence or retrogression, they may be removed.

According to Jackson and Coates[6] the best method of cure of multiple laryngeal papillomata is to scalp off the projecting parts of the growths, repeating the procedure as often as necessary.

If we can discover the cause of the change in characteristics of the infantile type to papilloma of the adult type, we may be able more successfully to treat these cases. With this thought in mind, it was attempted by Dr Holt, by the injection of the hormone testosterone, to bring on puberty in a small colored boy suffering from papilloma of the larynx, and although marked secondary changes were caused, the papillomata were not affected. It is common knowledge that some change takes place in the larynx at puberty. We know that a boy's voice changes; it becomes much lower in pitch, also the position of the larynx in the neck becomes higher. The change in voice is thought to be due to a sudden increase in the size of the larynx, along with the lengthening of the vocal cords.

Lewis noted that local applications of estrogenic hormone will bring about a definite change in the vaginal mucosa of young girls, from a simple squamous epithelium to stratified epithelium, the adult type. TeLinde and Brawner,[7] among others, confirmed this. Since treatment of laryngeal papillomata with testosterone was unsuccessful, it was thought that perhaps the local application of estrogens to the mucous membrane of the larynx in children suffering from papilloma might change the membrane from the infantile to the adult type, and thereby change the character of the growth from the infantile to the adult type.

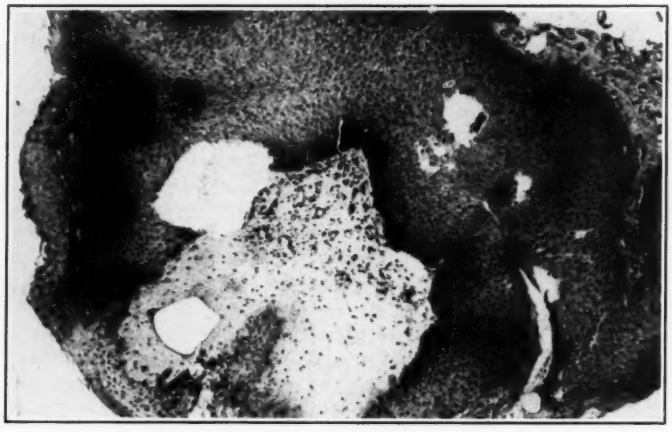

Fig. 1
Infantile papilloma.

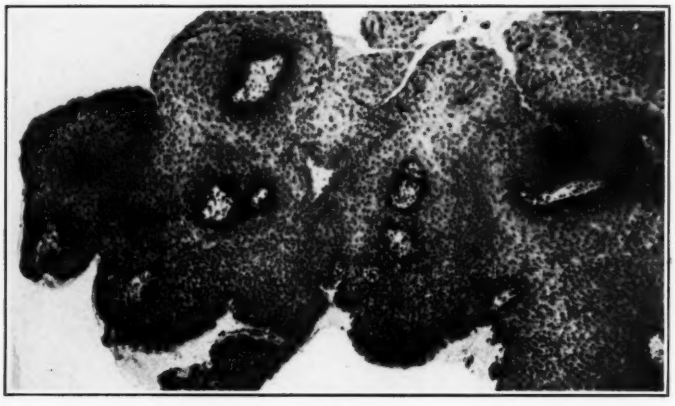

Fig. 2
Adult papilloma

Accordingly four cases of papilloma of the larynx then being treated by removal, and one new case, were treated by weekly applications of estrogenic hormone.* The applications were made through a direct laryngoscope or by spraying the solution directly into the larynx. Five cases were so treated.

The following is a brief review of the five case histories:

Case 1 (137091)—C. K., a white boy, unable to speak

"Amniotin" in oil, 10,000 international units per c. c., Squibb.

above a whisper since the age of two, was seen March 25, 1938, at the age of seven. With a direct laryngoscope the entire larynx was seen to be filled with papillomata. A tracheotomy was done and papillomata were removed on different occasions until February 29, 1939, when applications of estrogen were begun. This was applied five times and on examination of the larynx on March 31, 1939, there was only a small amount of papilloma left in the anterior commissure. The papilloma disappeared rapidly. On May 1, 1939, the patient was speaking in a clear voice and on re-examination October 13, only a small amount of granulation tissue was seen below the vocal cords. The larynx was otherwise perfectly clear. The patient was breathing well and the tracheotomy tube was removed on October 16, 1939. Estrogen treatment was discontinued. When he was seen January 5, 1940, the larynx remained free of papillomata. He was re-examined November 4, 1940, and a small papilloma on the right cord was removed

Case 2 (102852)—G. J., a colored girl, aged 5, was first seen March 17, 1937. A diagnosis of papillomata of the larynx was made. Tracheotomy was done March 19, 1937. The papilloma was removed on several occasions with very marked recurrence. The papillomata spread over the larynx and epiglottis and down into the trachea, so that breathing was becoming very difficult. Papillomata were removed from the trachea on three occasions. On February 27, 1939, applications of estrogen were begun and the throat sprayed at weekly intervals for five weeks. On March 31, the papillomata were not spreading, but were beginning to diminish noticeably by April 14, 1939. The papilloma was again removed July 28, 1939, and when the patient was seen December 29, the entire larynx was free from growths except for a small piece of pedunculated papilloma in the anterior commissure. This was removed and estrogen treatment was discontinued. The tube was removed, and the larynx was clear, February 12, 1940. On November 4, 1940, the larynx was still clear.

Case 3 (161408)—F. B., a white boy, aged 5, was first seen January 6, 1939, with a diagnosis of "web of the larynx." Examination of the larynx with a direct laryngoscope under general anesthesia failed to disclose any web, but showed both cords covered with papillomata. This tissue was removed and the patient had an application of estrogen. A small amount of papillomatous tissue was again removed July 5, 1939, at which time estrogen was applied to the larynx. This was repeated in October and November. The larynx was now practically clear. The tissue removed on the last occasion showed no papilloma, but a polyp. When last seen, December 29, 1939 (now six years old), the patient's larynx was clear. Estrogen was discontinued. On November 4, 1940, the larynx was clear.

Case 4 (146031)—J. S., a colored girl, aged 6, was first seen July 1, 1938, when she was admitted to the hospital with a diagnosis of papilloma of the larynx, to have a tracheotomy performed. A papilloma was removed August 12, 1938, and on two other occasions, and beginning February 24, 1939, the patient had estrogen sprayed in the larynx. When examined with the direct laryngoscope, March 27, she showed very little papilloma remaining in the larynx, not enough to remove. She had in all, eleven applications of estrogen and when examined November 19, 1939, the larynx was perfectly clear. Estrogen was discontinued. On November 4, 1940, her larynx was clear.

Case 5 (10448)—A. C., a white girl, aged 7, was first seen April 5, 1937, with a diagnosis of papilloma of the larynx. A tracheotomy was done on April 16, 1937. Papillomata were removed on many occasions, and the growths were fulgurated on February 11, 1938. A large mass was removed again January 11, 1939. On January 27, 1939, estrogen treatments were begun, the larynx being sprayed with estrogen on ten occasions. A papilloma was removed again May 22, 1939, and on October 6, 1939, the larynx was clear except for a small amount of tissue near the anterior commissure. The larynx was clear on December 29, 1939. Estrogen was discontinued. The larynx was clear, and tube removed, February 12, 1940. On November 4, 1940, the larynx was clear.

The fact that all the cases, although they were of different ages, 6, 8, 8, 9, 10 years, cleared up in about the same time, that is, in around six months, and in one case a papilloma changed into a polyp, seems significant. No secondary sex changes were noted. One case (*Case 1*) has had a small recurrence in the last six months.

Papillomatous disease of this style is self-limiting and the end of the disease was reached in these cases by unknown changes, but all five cases cleared up in about the same time, all having been treated about the same length of time.

Not enough hormone was applied to bring about any constitutional changes. An estimated 1,000 International Units or 0.1 c.c. of the preparation were applied at each treatment.

Many kinds of treatment have been used in papilloma of the larynx: excision, x-ray or radium, fulguration, local applications of chemical caustics and local and subcutaneous use of testosterone, none being satisfactory.

This report is made to present our observations. At this point in the investigation, the local application of estrogenic hormone seems to have a definite action on the multiple papillomata of children, changing the characteristics of the growth from infantile to adult type and making the treatment simple and far more satisfactory than in those cases of the same disease that have been seen in the past.

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DISCUSSION (*Abstract*)

Dr. Francis E. LeJeune, New Orleans, La.—I know of no condition within the larynx of a child, with the possible exception of stenosis of the larynx, which taxes the ingenuity, patience and courage of the surgeon more than do multiple papillomata of the larynx. All methods recommended for their treatment have been used with most indifferent success. Two of my cases merit brief mention. One was a child in whom thirty-five operations were performed for the removal of papillomata of the larynx. The other was a child seen at the age of 3 and treated over a period of eighteen years, during which time 103 operations were performed for removal of multiple papillomata from the larynx, trachea and right main bronchus. The papillomata extended to the bifurcation and had invaded the right bronchus. At the age of 21 they underwent degeneration into a malignancy and the boy died shortly afterwards. It is most interesting to know that he had multiple papillomata throughout a period of eighteen years, and everything we did could not arrest their growth, development and progress.

It has always been a source of wonder and amazement to me that a case of multiple papillomata may be operated upon and the papillomata removed on two or three occasions with complete recovery. A similar case in every respect again presents itself and repeated operations fail to eradicate the growth permanently. In other words, the two cases are similar in every respect, but one will continue recurring.

Since I received Dr. Broyles' paper a new case of papillomata of the larynx came into my office and I was able to use, after the removal of the papilloma, the estrogenic hormone locally upon it. We are going to make every effort to continue using it over a period of time, hoping to obtain as good results as Dr. Broyles reports.

I must disagree with one of Dr. Broyles' statements. He said that multiple papillomata did not recur in adults. My experience in adults is that they do occasionally recur, not with the same rapidity and to the same extent that we see in children, but I have under my care at the present time three adults who have had multiple papillomata of the larynx to my knowledge for ten or fifteen years, and every three or four years they need cleaning up. This has been going on for a long period of time.

Dr. Murdock Equen, Atlanta, Ga.—Dr. Broyles has shown us very interestingly the method of handling the perplexing problem of papillomata in children at Johns Hopkins Hospital. There is no laryngeal problem that receives such different methods of treatment in the various clinics, each one naturally thinking his method the best. This divergence of opinion is probably due to the ignorance of the etiology of papillomata and when the cause is found perhaps then its prevention may be possible.

Only upon one point do all agree and that is that dealing with any laryngeal growth the most important point is to bear in mind the preservation of the voice. So, if surgery of any type is used the preservation of the normal cord structure should always be attempted. I have found frequent scalping to be the method of choice. It is a well-known fact that papillomata may subsequently become malignant, but I have never seen such a case.

Jackson has said that x-ray may cause a necrosis of delicate laryngeal cartilage with resulting destruction of the entire larynx, so this procedure is to be followed with a great deal of caution both in the treatment of laryngeal papillomata and malignancy.

The method suggested by Dr. Broyles certainly gives promise of revolutionizing the treatment of papillomata of the larynx, if the results obtained in a large number of cases are similar to those he reported today.

Dr. M. F. Arbuckle, St. Louis, Mo.—My associate, Dr. A. C. Stutsman, and I have had the opportunity of treating only two or three cases of this type. I have been struck with the fact in one case, for example, under our observation over a period of twelve or thirteen years in which we have had to remove papillomata at the rate of once every month or six weeks, we have been able to avoid operating since last spring. I assume this is the result of our having given the patient the hormone. After a few doses of hormone her change from that of a baby-like child to definite adolescence was very striking both in appearance and in action. She will now sit up and let us look at her larynx without hesitation, whereas before she was a frightened baby.

We have a second case under treatment with Dr. Wm. L. Hanson, of East St. Louis, Illinois, in which the papillomata had been transplanted and were growing in several places in the pharynx when the child first came to our office. These tumors are getting smaller with the application of the hormone. A tumor growing from the posterior wall of the pharynx was as big as the first joint of a man's thumb. We purposely did not remove it because of its advantageous location for observation.

The late Dr. Lynch had a patient in whom during an emergency bronchoscopy papillomata were transplanted from the larynx down the trachea to its bifurcation.

Last summer while in New York Dr. Hayes Martin told me of his use of hormones in the treatment of juvenile tumor in the nasopharynx, and while this subject is not up for discussion at the moment, it is interesting to me to note the parallelism in many ways between this and papilloma of the larynx.

Dr. Broyles (closing).—We must remember first that the papilloma is not an invading tumor; it is limited to the epithelium and it has always been my impression, Dr. LeJeune, that in recurring papilloma of adults all the papilloma was not removed. We always try not to remove muscle from the vocal cords in removing papillomata.

THE TREATMENT OF CANCER OF THE LARYNX*

By CHEVALIER L. JACKSON, M.D.
Philadelphia, Pennsylvania

At the outset let us say that success in treatment will depend on early and accurate diagnosis.[1] Let us emphasize the fact, therefore, that the diagnosis should be made at the earliest possible moment, and confirmed by biopsy.

Much has been written about the relative advantages of irradiation and surgery in the treatment of cancer of the larynx. The relative radiosensitivity of different tumors as determined by their histopathology has been emphasized by some, and discounted by others, but most are agreed that a more important consideration in the selection of treatment is the gross location and extent of the lesion. Another factor closely related to this one, in the case of cordal lesions, is the degree of motility or fixation of the cord. The relatively high operability and curability of laryngeal cancer is due to the fact that it frequently begins on the true vocal cords, in what may be called the "anterior intrinsic area," a region poor in lymphatics and hence one from which metastasis is late. Cordal cancer has been called by the French laryngologist, Hautant, "un bon cancer."

Surgical Indications.[1]—(1) Lesions occupying the middle third of one vocal cord are suitable for the operation of laryngofissure by the "clipping" technic, regardless of histologic character or grading (*Fig. 1*).

(2) Lesions reaching the anterior commissure and even involving the opposite cord are amenable to extirpation by the laryngofissure route also, but in such cases the Chevalier Jackson "anterior commissure" technic should be used.

(3) Lesions in which the growth is cordal, but has reached the posterior end of the cord and produced impairment of motility, or has extended subglottically, call for total laryngectomy (*Fig. 2*).

Laryngectomy and partial pharyngectomy are also done in cases where the lesion is "extrinsic," but the results of operation in these cases are very unsatisfactory, and it is probable that irradiation would accomplish as much in arresting the growth and prolonging life.

Indications for Irradiation.—Certainly the development of "protracted fractional x-ray therapy" by Coutard[2] gave a new impetus to the treatment of laryngeal cancer by irradiation. The use of the "radium bomb" by Pfahler[3] has also produced good results. The implantation of radium and radon seeds as advocated and practiced by Quick,[4] Hayes Martin[5] and others has been especially useful in the treatment of cervical metastases. It is now our practice to use protracted fractional irradiation in the following cases:

(1) Cases unsuitable for laryngofissure in which laryngectomy is contraindicated by the age, temperament or physical condition of the patient. These factors would rarely if ever contraindicate the less radical procedure of laryngofissure, but they are to be regarded as relative contraindications to laryngectomy.

(2) Cases in which the lesion has reached the posterior extremity of the cord, but the cord is not fixed. It is the consensus of opinion at the present time that impairment of motility lessens the prospect of cure by irradiation. (Patients in this group may, of course, be treated by laryngectomy instead of by irradiation if they are willing, and if they are good surgical risks.)

(3) "Inoperable cases," in which the growth is extrinsic by origin or extension, or in which there are cervical metastases (*Fig. 1*).

By and large, it must still be admitted that surgical treatment has the best statistical results to show, and we feel that in early intrinsic lesions, especially if of well differentiated histologic character, operation should be done; but there certainly are cases in which the patient may be allowed to choose, or the laryngologist may even feel justified in advising, irradiation. There are those who minimize the importance of histopathology, but I believe that we are safe in saying that the ultimate prognosis will be most favorable in the better differentiated, slower growing, lower grade tumors, regardless of the method of treatment. Furthermore, I believe that "grading" should be taken into consideration, along with the other factors, in the selection of treatment in borderline cases; and in the less differentiated, "higher grade" tumors we should feel inclined toward more radical surgery, or toward irradiation, rather than toward conservative operations, but at the same time these tumors are to be regarded as of poor prognosis by any method of treatment.

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Thirty-Third Annual Meeting, Memphis, Tennessee, November 21-24, 1939.

LARYNGOFISSURE

"Laryngofissure" means simply splitting of the larynx, and for this reason some object to the application of the term to the operation for removal of a part of the larynx for early cancer. Hayes Martin,[5] for example, prefers to call all such operations partial laryngectomies. Another objection to the term is that it implies splitting the whole larynx, and for this reason the term thyrotomy has been used. The objection to the term thyrotomy, that it could be taken to refer to section of the thyroid gland, led to the suggestion of thyrochondrotomy.

Whereas Desault (1812) had suggested this operation rather for the removal of impacted foreign bodies than for the removal of growths, Brauers, of Louvain, first performed a laryngofissure for access to a growth, in 1833. He cauterized a papillomatous tumor in a male 40 years of age, and the patient survived for twenty years. Gurdon Buck of New York was the first to do the operation of laryngofissure for a malignant growth (1851). There followed in the next few years an increasing number of attempts to utilize the laryngofissure approach, a considerable impetus being given by the discovery and development of laryngoscopy (1855). However, the early results were very unsatisfactory, as shown by von Bruns (Berlin-1878), who reported a series of 19 cases, in which only two patients survived one year! The British laryngologists, including Morrell Mackenzie, and even Butlin and Semon, later the outstanding exponents of laryngofissure, joined in condemning it at this time. The bad results were due to use of the procedure in advanced and unsuitable cases, as well as to faulty technic. After 1890, both Butlin and Semon, working first together and later separately, steadily improved their results, and the operation was reinstated in its proper place. Other pioneers whose statistics began to

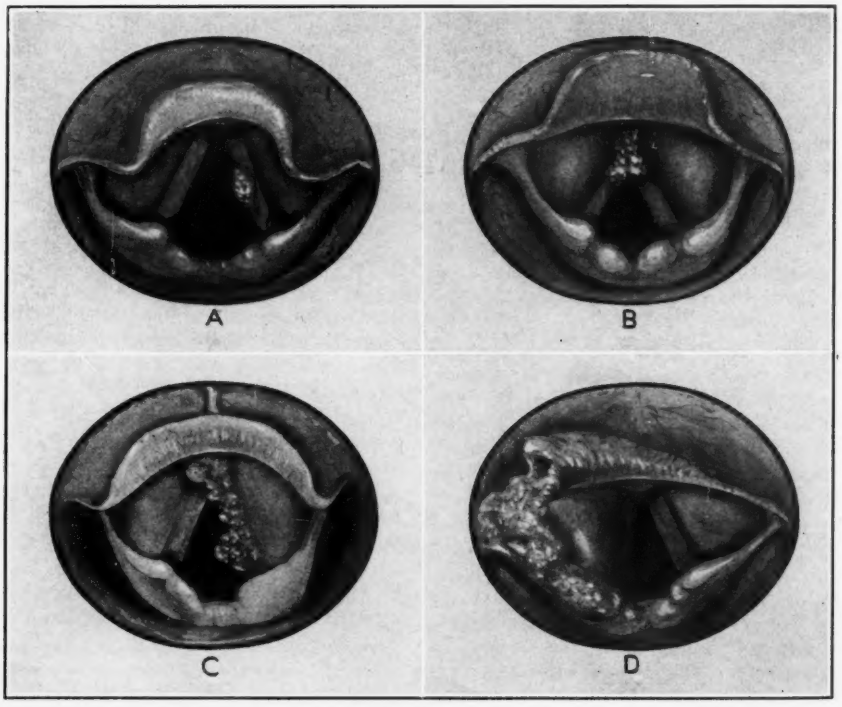

Fig. 1

Laryngoscopic views showing: (A) lesion ideal for treatment by laryngofissure, using the "clipping" technic; (B) lesion requiring the use of the "anterior commissure" technic of laryngofissure; (C) lesion involving the entire vocal cord, requiring total laryngectomy or irradiation; (D) extrinsic lesion involving epiglottis and aryepiglottic folds, which would call for treatment by irradiation as the procedure of choice. (*From Jackson and Jackson, Cancer of the Larynx, W. B. Saunders Co.*)

show what could be done by laryngofissure in properly selected cases were Schmiegelow, Chiari, Moure, Delavan, St. Clair Thomson[6] and Chevalier Jackson.

Technic.—The technic of laryngofissure used in the Temple University Clinic at the present time is as follows [1 7]:

(1) *Anesthesia.*—Local anesthesia by infiltration with novocain 1 per cent, intradermatically and then subcutaneously along the midline of the neck is used in all cases. The local anesthesia is completed by topical application of cocaine 10 per cent (or pontocaine 2 per cent) to the interior of the larynx and upper trachea on a swab introduced through an incision in the cricothyroid membrane. This application is analgesic, and eliminates the cough reflex from the larynx and upper trachea while conserving it in the lower trachea and bronchi; also, it produces slight ischemia of the mucous membrane and soft tissue of the interior of the larynx, lessening the tendency to hemorrhage.

(2) *The Incision.*—A straight vertical midline incision from the thyroid notch to just below the level of the cricoid is used. If tracheotomy is to be done, the incision may be prolonged downward to the suprasternal notch, but we do not do tracheotomy as a part of the standard operation.

Chevalier Jackson has emphasized the importance of not skeletonizing the larynx in laryngofissure, because of the unnecessary trauma thus inflicted on the external perichondrium and consequent impairment of nutrition of the thyroid alae.

(3) *Special Cover.*—As soon as the incision has been made, the thyroid and cricoid cartilages exposed, and hemostasis accomplished, a special cover consisting of a sheet with an opening in it just big enough to fit the wound is put in place, the edges of the opening being clipped to the skin margins. This cover helps to avoid dermal contamination during the remainder of the operation, and particularly during the manipulation of the cartilages.

(4) *Incision of Cricothyroid Membrane.* After placement of the special cover, the cricothyroid membrane is incised, either transversely or vertically, for the topical application of cocaine to the interior of the larynx. At first a few drops are squeezed out by pressure of the sponge against the borders of the incision, and then the sponge itself is gently introduced. Several successive applications are made in the same way (*Fig. 3*).

(5) *Division of the Thyroid Cartilage.*—In cases where the lesion does not reach the anterior commissure, the "clipping" technic is used, dividing the thyroid alae exactly in the midline with the turbinotome, but in cases where the lesion reaches the anterior commissure, the special technic for such cases first described in 1922 by Chevalier Jackson[8] is preferable (*Figs. 4* and *5*). The essential feature of this technic is division of the thyroid cartilage from the outside by means of an electrically driven circular saw, or in the case of patients with a very soft cartilage, a knife, this incision not going clear through the internal perichondrium. In this way we avoid cutting through the tumor, which is always to be avoided if possible. In a recent series of 50 cases, the clipping technic was used in thirty-two cases and the Jackson "anterior commissure" technic in eighteen.

(6) *Inspection of Interior of Larynx.*—If the patient has been properly studied beforehand by

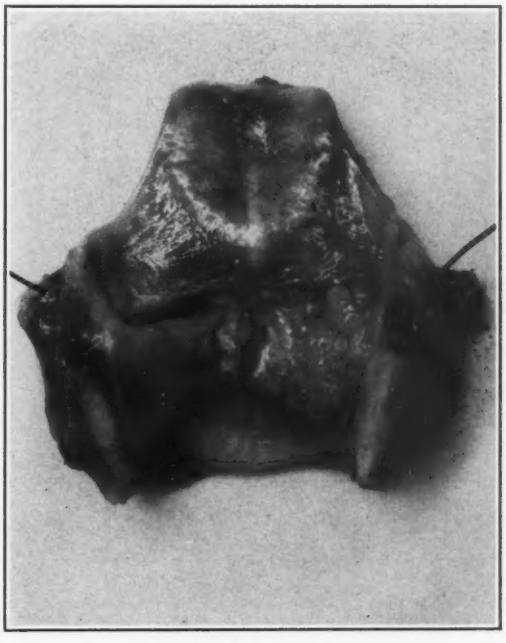

Fig. 2

Subglottic cancer of the larynx for which laryngectomy was done. Lesions of this kind cannot be satisfactorily extirpated by laryngofissure and the results of irradiation are not good (see Fig. 9 A).

direct as well as indirect laryngoscopy, one should have a very accurate idea of the location and extent of the lesion, but after the larynx is opened it should again be carefully examined before the excision is begun. In the clipping operation this is simple, but in the anterior commissure operation it is a little more difficult. In the former, we can inspect the lesion before doing even the subperichondrial dissection, but in the anterior commissure cases it is necessary first to separate off the internal perichondrium on both sides and then to section vertically the less involved cord and ventricle so that it can be reflected in such a way as to permit good visualization of the entire interior of the larynx.

This careful inspection permits one to decide upon the extent of excision necessary to give a safe margin of normal tissue around the growth. I have, in a number of cases, removed only one cord and part of the ventricle, leaving the ventricular band untouched. I believe it permissible to do this in the very limited cases, though Sir St. Clair Thomson, Negus, and some others feel that one should always take out both the true and the false cord, with the ventricle between.

(7) *Partial Removal of Cartilage.*—We do not resect the cartilage. Lack advocated resection of the thyroid ala along with the soft tissue bearing the growth, because he believed that it was easier to be sure of adequate removal in this way. St. Clair Thomson[6] has made it a part of his technic to do a subperichondrial resection of the thyroid ala before excising the tumor and adjacent soft tissue.

(8) *Excision of the Growth.*—After subperichondrial dissection the tumor-bearing mass is excised with special curved scissors, including generally the tip of the vocal process of the arytenoid on the more involved side. If possible, the mass excised is kept in one piece, but of course it may be necessary to remove additional tissue if it is found that the margin is insufficient on one side or the other. To take a full centimeter of normal on all sides is ideal, but not always practicable (*Fig. 6*).

(9) *Hemostasis.*—Plain or iodoform gauze is tucked into the open larynx immediately after the excision, while the operative specimen is inspected, and most of the bleeding will generally stop with this alone. If a spurting vessel can be caught quickly with a hemostat, so much the better, because later it may retract and be difficult to find. The larynx must be got absolutely dry before closing, or postoperative bleeding will be sure to occur.

Fig. 3

The operation of laryngofissure. The larynx has been partially skeletonized, but great care taken not to denude the thyroid cartilage of external perichondrium. The cricothyroid membrane has been incised preliminary to the division of the thyroid cartilage. Cocaine 10 per cent or pontocaine 2 per cent is applied topically through this incision in order to anesthetize the interior of the larynx and the upper trachea. The next step would be division of the thyroid cartilage by means of shears if the "clipping" technic is used or by the circular saw if the "anterior commissure" technic is used. Note special cover which is attached to the skin margins as soon as the skin has been incised and hemostasis accomplished.

If the excision has been rather extensive, including one or both ventricular bands, the base of the epiglottis will be left without support and should be stitched forward as suggested by Gabriel Tucker.[9] This will tend to prevent stenosis anteriorly.

(10) *Closure.*—No sutures are put through the perichondrium or cartilage, though a suture or two may be used in closing the incision in the cricothyroid membrane. The fascia and

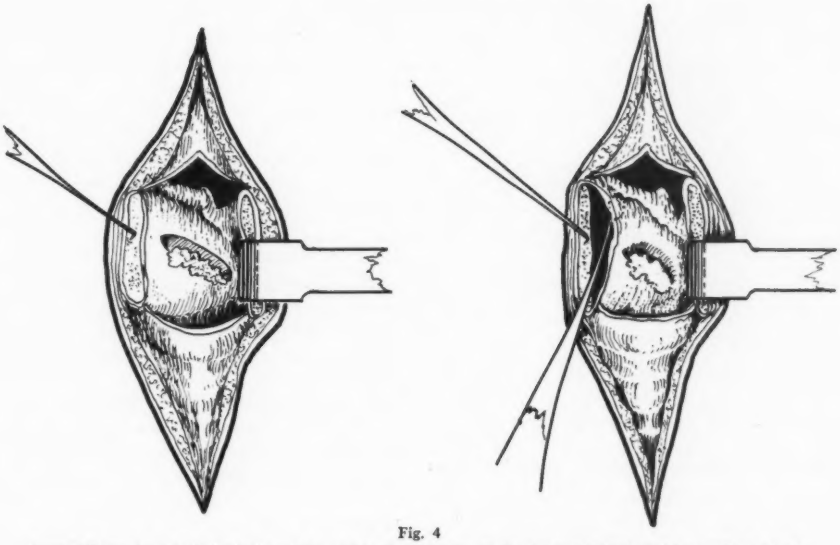

Fig. 4

Laryngofissure by the "clipping" technic. Note the exposure of the lesion obtained and the method of subperichondrial dissection used. (*From Jackson and Jackson, Cancer of the Larynx, W. B. Saunders Co.*)

muscles are closed with buried sutures (alloy steel wire) and the skin with Michel clamps. No drainage has been used for the past several years, though in the earlier cases a small wick of iodoform gauze was left in the lower end of the wound.

(11) *Dressings.*—A plain flat gauze dressing is applied, the first layer moistened with 1:10,000 bichloride of mercury solution or compound tincture of benzoin. The dressings are changed daily, and the clips removed on the third or fourth day.

After Care and Course.—The patient is kept sitting up, or rather with the head of the bed elevated. He is instructed not to talk, but to use pad and pencil to express himself. After a few hours he is given liquids and soft solids, being encouraged to sit up, lean slightly forward and take a good swallow, rather than sipping or taking the liquid through a glass tube. In none of our cases has a feeding tube been necessary, but if an extensive excision is made, and especially if a large portion of the arytenoid is removed, it may be necessary to use one. Opiates are contraindicated and only the very mildest sedation is permissible.

The wound is generally healed externally in

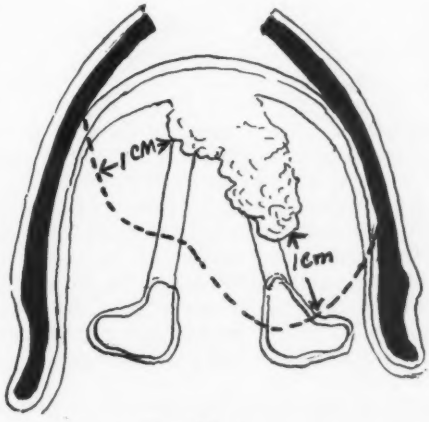

Fig. 5

Laryngofissure by the "anterior commissure" technic. After division of the thyroid cartilage from the outside, using the circular saw, the soft tissues are separated, by subperichondrial dissection, from the inner surfaces of the thyroid alae; then the less involved cord is divided and reflected in such a way that a thorough inspection of the interior of the larynx is permitted before the completion of the excision of the tumor and a sufficiently wide margin of surrounding normal tissue. The vocal process of the arytenoid cartilage is generally included in the tissue removed on the more involved side. (*From Jackson and Jackson, Cancer of the Larynx, W. B. Saunders Co.*)

Fig. 6
Carcinoma of the middle third of the right cord removed by laryngofissure. In such an early and limited lesion as this it is possible to accomplish a permanent cure by removal of the cord alone (see Fig. 7 A).

four or five days, but the healing of the interior takes several weeks. Most patients are discharged from the hospital in from one week to ten days.

Results.—In a previous paper[10] a series of one hundred and eleven patients operated upon before 1930 was reported, and these patients were divided into two groups, those in which the lesions were entirely suitable for laryngofissure and those in which the lesions were not suitable, but in which the operation was done because it was the patient's choice. Of the suitable group, sixty-two survived operation and were traceable, not dying of any other disease in the three year period, and fifty (80 per cent) were living and free of recurrence. Of the twenty-three unsuitable cases, out of thirty-one that were surviving and traceable, only eleven (47 per cent) were living and free of recurrence at the end of three years. Adding to the sum of these two groups the number of patients having laryngofissure since 1930, or ninety-one, we have a total of two hundred and two patients upon whom laryngofissure has been done, but the total number of traceable patients surviving operation and not dying of intercurrent disease for at least three years would be one hundred and thirty-five. Of these, one hundred and eleven or 82.2 per cent were cancer-free and apparently well at the end of three years. This figure includes all cases, suitable and otherwise.

In a series of fifty consecutive patients I have personally operated upon by laryngofissure since 1930[7] there has been no operative mortality; six patients have died of other causes than cancer, one of them surviving for four years, two for three years, one for two years and two for a little over one year. Only four patients in this series have developed recurrences, to my present knowledge, and one of these is still well, seven years after laryngectomy. Eight patients have survived cancer-free for five years and over, four for four years, four for three years, twelve for two years, and six for between one and two years. Since it is generally agreed that very little significance can be attached to statistics of cure for less than three years, let us add these first groups together, which gives us sixteen patients free of recurrence for at least three years out of nineteen, or 83 per cent.

Voice.—Curing the cancer is of course the first consideration, but next comes voice. Patients who have had one or both true cords removed by laryngofissure practically always develop a useful voice, but its quality, pitch, and carrying power vary greatly. Cicatricial "adventitious" cords develop in most cases, and in the patients who develop good voices, generally either one good cord remains, and a good "adventitious" cord has developed, with which it can approximate and vibrate; or two good "adventitious" cords have formed to replace two cords that have been removed (*Fig. 7*). Another mechanism by which a good voice can be produced is ventricular band phonation, which is to be regarded as undesirable when it is "usurpative," but which may afford an excellent and very efficient substitute for true cord phonation when one or both cords have been removed. The presence of a

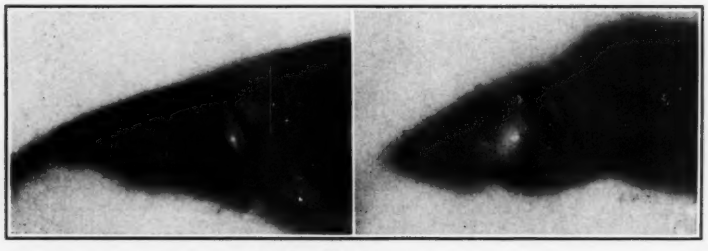

Fig. 7
Laryngoscopic photographs showing the postoperative results in two cases in which the right cord was removed four years and one and a half years previously. Both of these patients have developed very good voices.[11]

granuloma may interfere seriously with the production of a good tone, and such tissue should be removed by direct laryngoscopy if it does not shrink up and disappear in a month or two after operation. These granulomata have been noted in about 35 per cent of cases in our recent series. Sometimes several removals are necessary.

Of the fifty-one laryngofissure patients operated upon in the past ten years, who answered a questionnaire with regard to voice,[11] forty-three replied in the affirmative to the question, "Have you developed a useful voice since your operation?" In reply to the question, "Is your voice good, fair or poor?" eight replied "good," thirty-seven "fair" and six "poor." Thirty-seven of these patients stated that they had been able to resume the same work that they had done prior to operation. Sixteen patients could sing before operation, but only three claimed they could do any singing since the operation.

LARYNGECTOMY

Laryngectomy was first done for cancer of the larynx by Billroth in 1873, though the operation had been done a few times previously for other conditions. Billroth's patient died of recurrence seven months after operation. The first twenty-five years of the history of laryngectomy makes dismal reading, because the patients that survived the operation and escaped death from postoperative pneumonia almost all developed recurrence and died within a few months. Gluck reported an operative mortality of 80 per cent in his first ten cases, but in a later series of nine cases he had only about a fifty per cent mortality, and in 1914 he reported 72 cases with no operative deaths. Delavan at one time (1909) said: "Laryngectomy has added nothing to the sum total of human life," but later he took a somewhat more optimistic view. In 1922 MacKenty reported forty-six cases, all but two of them intrinsic, with an operative mortality of about 4 per cent, and his figures showed 66 per cent of patients free from recurrence for three years or more. Gordon New, in 1928, described a two-stage technic by which he had operated upon forty-two patients with operative deaths in two cases, both following the first stage.

In the past decade many operators have reported series of cases: Looper, Babcock,[12] Clerf,[13] Crowe and Broyles, Orton, Schall, Zinn and others. One of the most interesting recent developments in technic is that described by Crowe and Broyles,[14] subperichondrial dissection in the skeletonizing of the larynx. Other technical points stressed by these operators are the minimizing of tissue trauma and the overlapping of muscles in closure.

Recently, at the Clinical Congress of the American College of Surgeons in Philadelphia, Chevalier Jackson[15] stressed the advantages of the "narrow-field" as compared with the "wide-field" type of operation, and the question is also discussed in our recently published textbook.[1] Certainly the present trend in laryngectomy has been toward the "narrow-field" type of operation.

Technic of Narrow-field Laryngectomy.—The steps in "narrow-field" laryngectomy are as follows:

(1) *Anesthesia.*—Local anesthesia using infiltration of the tissues of the neck is sufficient, but the additional use of tribromethyl alcohol per rectum (60 to 80 mg. per kilogram of body weight) gives complete unconsciousness. It should be given about fifteen minutes before operation. In addition, morphine sulphate (0.01 gram, or 1/6 grain) may be given about an hour before operation and repeated if necessary.

(2) *Incision.*—A midline incision is made from the hyoid bone to the suprasternal notch. If the thyroid isthmus is high and thick it is divided and the ends are closed by stitching. If low, flat and small, as it often is, nothing need be done with it except to draw it downward. Skin flaps are not dissected back as in wide-field operating.

(3) *Skeletonization of the Larynx.*—Our object is to remove the larynx and as little else as possible, therefore the muscular insertions are separated from the perichondrium close to the cartilage. The sternothyroid and thyrohyroid muscles must be detached from the thyroid cartilage because we are going to take the larynx out, but there is no need to divide or traumatize the sternohyoid muscles; they can easily be retracted while operating, and they afford excellent support for the pharyngeal repair.

(4) *Ligation of Laryngeal Arteries and Cutting of Cornua.*—The strong rotation of the larynx with unilateral retraction will bring forward the superior and inferior laryngeal arteries, and the posterior edge of each thyroid wing in turn. The clipping of the cornua is to be done carefully to avoid perforation; the cut-off horns of cartilage are either left in their beds or subsequently dissected out.

(5) *Opening the Pharynx and Lifting the*

Larynx.—Before the pharynx is opened, the anesthetist must make doubly sure by aspiration that there is no accumulated fluid in the pharynx to flood the wound. An intranasal catheter may be inserted for this purpose. The thyrohyoid ligament is incised transversely, the tip of the epiglottis grasped, and the larynx brought forward. As soon as its hypopharyngeal wall is exposed this wall is stripped backward from a crescentic incision over the cricoid at the bases of the arytenoids (*Fig. 8*). In dissecting this wall loose the flap should be made as heavy as possible even to including the cricoidal perichondrium, for this is to form an important part of the pharyngeal repair.

(6) *Closure of the Pharynx.*—The pharynx should be closed in the form of an inverted "V" or "U," using interrupted 00 chromic catgut sutures, and including with each suture a little muscle tissue. Some fibers of the inferior constrictor, sternothyroid and thyrohyoid muscles may be brought in for additional support by a second line of sutures. Stiffening and strength can be greatly augmented if perichondrium has been included in the dissection of tissue from the cricoid and thyroid. A well supported, water-tight, air-tight suture line is the desideratum.

(7) *Amputation of the Larynx From the Trachea.*—The best tracheostoma is made by a ring-like horizontal slice of cricoid cartilage. If, however, this would leave insufficient normal margin below the growth, a tracheal ring must serve (*Fig. 9*).

(8) *Anchoring the Trachea to the Skin.*—The slice of cricoid or the tracheal ring is brought and sutured in place at the lower end of the midline incision. Four anchor sutures (alloy steel) are used and between each is put a fine approximating stitch to make close contact of skin to mucosa, in order to promote primary union and to prevent subcutaneous emphysema.

(9) *Closure of the Muscles.*—The sternohyoid muscles, which have been preserved intact are brought together, overlapped in the midline, and stitched with alloy steel wire or chromic catgut (00) as advised by Crowe and Broyles.[14]

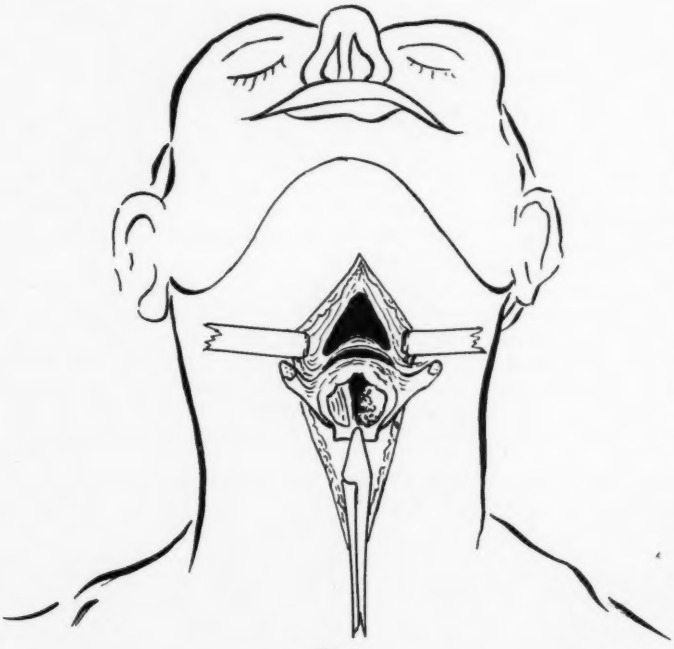

Fig. 8

Laryngectomy by the "narrow-field" technic. Note that a midline incision is used, and that the larynx is taken down from above. The trachea may be divided before the pharynx is opened, however, especially in cases where there is any degree of dyspnea. It is easier to denude the posterior surface of the cricoid cartilage and inner surface of the thyroid alae, by subperichondrial dissection, from below upward, but even if this is done, the pharynx is subsequently opened above, the epiglottis drawn forward, and the supraglottic region clearly visualized as the final incisions in the lateral pharyngeal and post-cricoidal mucosa are made.

(10) *Closure of the Skin.* A firm, neat, close approximation of the edges of the skin should be made with alloy steel wire sutures or Michel clamps. Primary union can often be obtained. In the case of mild infection it will still hold except where opened for drainage. Of course, virulent infection may require opening of the entire wound.

(11) *Drainage.*—A small glass or alloy steel sump (Babcock) is all that is necessary. It is laid in under the muscles before the skin is closed. A small catheter attached to a very low power electric motor is inserted in the sump for the first 24 or 48 hours to maintain constant slight suction. If preferred, of course, drainage tubes or sumps may be inserted through lateral in-

Fig. 9

(A) Patient ready for discharge two weeks after laryngectomy by the "narrow-field" technic. Note that quite a good tracheal stoma has been obtained, though in this case it was not possible to conserve a portion of the cricoid. (B) A patient in whom a particularly good stoma was obtained by the use of a portion of the posterior plate of the cricoid. This patient will not need to wear a tracheal cannula (photograph of larynx of patient A shown in Fig. 2).

cisions in order to allow the midline to close promptly and to prevent drainage into the tracheal stoma.

(12) *Dressings.*—A pad of gauze soaked in compound tincture of benzoin is laid on the suture line. A light covering pad of gauze is laid over all. A few turns of bandage are passed around the neck with efficient firmness to obliterate pockets, if any. Usually, in narrow-field laryngectomy, pocketing can be avoided. The laryngectomy cannula is now inserted, though if a good stoma is obtained the cannula may not be required.

Postoperative Care.—The patient usually shows no sign of shock. He should be disturbed only for necessary attention. He should sit up in bed the second day, and for a little while in a chair on the evening of the third day.

A well-balanced diet in liquid form is given through an ordinary nasal catheter inserted at the conclusion of the operation. Total fluid intake and output must be carefully watched. About the sixth or seventh day the catheter is removed and sterile liquids are given by mouth. The patient is constantly reminded by the nurse that he should not gulp. The liquids should be taken in small sips, and in about ten days soft solids may be taken, but only in small quantities, say a half teaspoonful at a time.

Results in Laryngectomy.—In our records we have data concerning one hundred and seventy-eight cases in which laryngectomy was done, by various operators, prior to 1938. In this series we find that 130 patients who survived operation were traceable, and did not die of other cause within three years, while fifty-six developed recurrences. Seventy-four, or 57 per cent, obtained at least a three-year cure. In evaluating this figure, two things must, of course, be borne in mind: first, some of the patients operated upon were known to be very poor operative risks, or to have lesions so extensive as to be regarded by many operators as inoperable, and second, it must be admitted that recurrences do occur after three years.

Speech After Laryngectomy.[11]—The patient who has had his larynx removed, or is about to have it removed, is apt to be very depressed at the thought that he may never be able to talk again, but he will be cheered up at once if you explain to him that the larynx is only one part of the speech mechanism; that it provides a col-

umn of air (coming up from the lungs) and a pair of vibrators (the vocal cords), but that it is the "moulds of speech" (tongue, lips, cheeks, palate, etc.) which form the words. Then you explain that it will be necessary for him to learn to collect air in his hypopharynx, esophagus, and stomach to replace the air column from the lung; and to produce tone by means of vicarious cords formed in the hypopharynx or pharynx. He will probably be very skeptical about this, but one can assure him that experience has shown us how to help patients get the knack of this sort of speech, and that his course of voice lessons will be begun as soon after operation as healing permits. Schall[16] has given us two excellent papers in which he has shown that the laryngectomized patient is "not a social outcast, nor in most cases is he an economic burden." Schall has found that these patients constitute "A most optimistic, cheerful group, neither objects of curiosity nor, in most cases, recipients of charity."

These views regarding the social and economic rehabilitation of the laryngectomized patient are fully supported by the replies to a questionnaire recently sent out to all of our patients operated upon for cancer of the larynx in the past 10 years. We received replies from thirty patients who had had laryngectomies, and of these, eighteen replied "Yes" to the question, "Have you learned to speak without your larynx?" Five stated that they could whisper; only six said flatly "No." As mentioned before, one of the most interesting things noted in the replies to the questionnaire was the fact that in reply to the question, "Is your voice good, fair, or poor?" fifty per cent of the laryngectomy patients replied "good," while only a little over ten per cent of the laryngofissure patients replied "good," most of them saying "fair." The occupations of the patients who had laryngectomies were as follows: salesmen, merchants, carpenters, army officers, physicians, laborers, steam fitters, molder, housewives, locomotive engineer, wood carver, magistrate, executive, printer, tailor, hotel proprietor, waiter, gate-tender, and milkman. Seventeen of these patients have been able to resume the same work, wholly or partially. Among the questions asked the laryngectomized patients was whether or not they had tried to use an artificial larynx and whether it had proven satisfactory. Only eight had tried it, and of these only two had found it satisfactory—one other said "fairly so," and still another "yes and no."[11]

Morrison[17] deserves a great deal of credit for advocating a definite course of voice instruction for laryngectomized patients. Some will not require any lessons, but most will make little progress or develop hopelessly bad habits if they are not systematically taught. We have, for the past several years, made it our practice to begin voice lessons in each case as soon as the condition of the wound will permit, and the results have been very gratifying.[11]

With regard to the artificial larynx, I believe it is a mistake to have the patient try it before he has had a chance to develop a bucco-esophageal voice. I believe its use should be reserved for those who are not able, after a fair trial, to develop this more natural kind of speech.

Technic of Irradiation.—I have already discussed the indications for irradiation in cancer of the larynx, and it may be of interest to outline the technic of protracted fractional x-ray therapy that has been used by Dr. W. Edward Chamberlain at the Temple University Hospital during the past ten years. Of course, this technic is varied slightly from time to time, and individual cases are treated according to indications as they develop, but an outline of the treatment given in an average case is as follows: one hundred and twenty-five roentgens daily to each side of the neck for twenty-five treatments, using a skin portal of seven to ten centimeters and a skin target distance of fifty centimeters. The factors commonly used are one hundred and eighty kilowatts, eight milliamperes, and filtration with two millimeters of copper and one millimeter of aluminum. Ten and six-tenths roentgens per minute are given for about eleven and eight-tenths minutes to each side. A total dosage of three thousand roentgens or slightly more is delivered to each side.

In cases with metastatic nodes, protracted fractional irradiation should be supplemented by interstitial irradiation, using radon implants, as advised by Quick[4] and Martin.[5]

Results from Irradiation.—Most of the patients treated with irradiation in our clinic have been postoperative cases, but thirty-seven patients were treated by irradiation alone between 1930 and 1937. Of these, four were lost track of, and eighteen developed recurrences in less

than three years, leaving fifteen (or 45 per cent) in which at least a three-year cure was obtained. However, very little assurance of the permanence of a cure by irradiation can be taken from a three-year survival without evidence of disease, for recurrences may occur in five years or longer. Of course, after the lapse of one year some additional irradiation may be given if needed. The giving of additional irradiation sooner than this is contraindicated, because the skin and other normal tissues will not tolerate it.

It is to be expected that the end results of treatment by irradiation alone will improve as our knowledge of the indications and technic of this method improve.

Voice After Irradiation.—Certainly the results with regard to voice are better after irradiation than after any surgical procedure. The voice may be expected to return completely to normal, or to almost normal, but this must not lead us to choose irradiation if the ultimate prognosis as to cure of the disease and preservation of life is not so good, unless operation is for some reason contraindicated, or is refused by the patient.

CONCLUSIONS

(1) The treatment of a cancer of the larynx should be undertaken only after a biopsy-proven diagnosis has been made.

(2) Laryngofissure is the treatment of choice in anterior intrinsic cordal cancer, using (a) the clipping technic if the lesion involves only the middle third of the cord, and (b) the Chevalier Jackson anterior commissure technic if the lesion reaches the anterior commissure. The operation of laryngofissure should give over 80 per cent cures in suitable cases.

(3) Laryngectomy is indicated if the lesion involves the arytenoid region, with impairment of motility, or if it extends subglottically. Attention is called to the recent trend toward a "narrow-field" type of operation. The operation of laryngectomy should have a very low operative mortality, and should give at least 50-60 per cent cures in advanced intrinsic cases beyond the possibility of cure by laryngofissure.

(4) Irradiation, by the protracted fractional (Coutard) technic or by radium bomb may be used instead of laryngectomy in cases where the posterior extent is a little too great for laryngofissure, but preferably when the cord is not fixed. It may also be used when operation is refused, or when the patient's age, temperament or general physical condition contraindicate operation, and in extrinsic inoperable cases. In a small series of cases treated by x-ray alone a three-year cure was obtained in 45 per cent.

(5) Histopathology should be studied and recorded. It is of particular value in the selection of treatment in borderline cases. Tumors of well differentiated "low grade" type are probably of the best prognosis, whether treated by surgery or by irradiation, but we always consider surgery as the first choice in such cases, provided there is no contraindication.

(6) Curing the cancer is the first consideration in treating cancer of the larynx, but the second consideration is voice. After laryngofissure, the patient will have a useful voice, but its tone quality and carrying power cannot be guaranteed. The bucco-esophageal voice that can be developed after laryngectomy is quite satisfactory and vastly preferable to the voice produced by the artificial larynx. While this bucco-esophageal voice is picked up spontaneously by many patients, systemic instruction is of great help. The voice after treatment by irradiation will be best of all, but this fact should not lead us to give this treatment when surgical extirpation is indicated.

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Temple University Hospital

DISCUSSION (*Abstract*)

Dr. Francis E. LeJeune, New Orleans, La.—Dr. Jackson stated that when considering irradiation for carcinoma of the larynx he was guided by whether or not there was motility of one cord. I should like to know why he has come to that conclusion.

I personally do not like irradiation in these cases if surgery is at all possible. I have used irradiation in cases which had progressed beyond the limits of surgery with good results.

Dr. Jackson said that when doing a laryngectomy the cricoid cartilage is frequently left in place in order to retain a good plastic opening of the trachea. I have always removed the cricoid when doing a laryngectomy and I want to be sure that I have understood him correctly. I can well see the wisdom of leaving it in certain cases.

Dr. Murdock Equen, Atlanta, Ga.—I should like to ask Dr. Jackson if in performing laryngofissure operations he has ever used a dental electric saw in going through the thyroid cartilage. This instrument is much smaller than the pistol shaped handle advocated by Halle and is more easily controlled.

I should also like to ask Dr. Jackson how often he sees patients in whom it is absolutely impossible to get a satisfactory laryngeal view on mirror examination. Recently, we had such a case, a woman weighing over two hundred pounds, and in spite of cooperation and cocainization we could get no more than a fleeting view of her vocal cords and then for not long enough to be sure of the origin of the intralaryngeal new growth. The patient was given sodium ethyl thiobarbiturate intravenously for relaxation so that a direct laryngoscopy could be performed. This failed to relax her and it was supplemented by ether with the same results. The relaxation was not sufficient to permit the passage of the laryngoscope. The patient was sent back to her room and permission was granted to open her larynx (thyrotomy) for examination. The thyroid cartilage was opened in the midline and we found that we had cut through the middle of a new growth, thus making it impossible to perform Jackson's anterior commissure operation. A biopsy was taken and the patient was again returned to her room. The pathologic study showed the process to be a carcinomatous one, grade II.

Dr. Jackson, in your opinion what is the proper procedure from this point? Should we use extensive x-ray therapy or should the larynx be removed?

I might add that one month following this discussion the patient developed marked dyspnea. Her larynx was removed and it was found that the rapidly growing carcinomatous process had completely obstructed the lumen. She has made an uneventful recovery.

Dr. George J. Taquino, New Orleans, La.—I should like to ask Dr. Jackson if he still uses his central incision, cutting through the thyroid cartilage without cutting through the perichondrium and then elevating the perichondrium on both sides? Does he then make a central incision through the perichondrium without cutting through the anterior commissure or does he prefer making the incision on the unaffected side? If so, what are the advantages of this L-shaped incision over the middle line incision?

Dr. C. C. Cody, Houston, Tex.—The Chair would like to ask if Dr. Jackson has found any use for sulfanilamide for the purpose of cutting down and preventing infection of the wound.

Dr. Jackson (closing).—In reply to Dr. LeJeune's questions, the matter of motility has rather a bearing on the prognosis of treatment by irradiation than on the prognosis of treatment by surgery, as I see it. I do not believe that the patients with impaired motility do any worse than others if treated by laryngectomy, but the patients treated by irradiation definitely do better if the cord is still freely movable.

That is not an original idea with us. It is one which has been expressed by many of the men who have treated large numbers of patients by irradiation, and it is a view which we have not accepted blindly, but which our experience tends to confirm. The patients who have done best under irradiation, when they for one reason or another have been treated in that way rather than by laryngectomy, have done better if the cord was not fixed. So that while I would agree with the Doctor—could I at this point ask Dr. LeJeune to tell me if I am answering his question? Would he repeat it very concisely?

Dr. LeJeune.—You are right. I wanted to know why it was. I do realize that if the cord is fixed the lesion is much more extensive, but I wanted that particular thing brought out.

Dr. Jackson.—You stated your preference was for laryngectomy in both cases.

Dr. LeJeune.—I would do laryngectomy when the cord is completely fixed. I would not consider it if the cord were still movable.

Dr. Jackson.—Dr. LeJeune has expressed it the same way that I did, and yet I would consider laryngectomy even in cases where it was freely movable if there were no other reason to swing us toward irradiation.

I have at the present time a good illustration of this problem under treatment, a man of 70 who had a lesion involving a whole cord, but in which there was no apparent impairment of motility. Grossly it was a little too far back to make it a good case for laryngofissure. The histopathology showed a grade 3. I regard this

kind of case as relatively favorable for irradiation and in view of the patient's age, the extent of the lesion posteriorly and the histology, I have put him on a regime of x-ray therapy.

As I said at the beginning of this discussion, the matter of motion or lack of motion affects rather the prognosis of treatment by irradiation than the prognosis of treatment by laryngectomy.

In regard to the cricoid, the point there is that if you can save the cricoid or part of the cricoid, it will help very much in maintaining a stoma which does not require the wearing of a cannula. In the great majority of our cases of laryngectomy we have been able to preserve at least a portion of cricoid, and in those cases we have not had to use a tube. If a patient can get along without his crutches, he prefers to get along without them.

In regard to Dr. Equen's question, I have not used the instrument of which he spoke. I should be interested in seeing and trying it as he suggests.

As to the patients in whom we cannot visualize the larynx with a mirror, they are very, very few (adults), but there are some. The technic of mirror laryngoscopy is something that seems to be poorly understood by many laryngologists. By this I do not mean Dr. Equen. Cases such as he described are just the cases in which we should be first to say that direct laryngoscopy was necessary, and in some cases the anatomy would make satisfactory visualization even by the direct method difficult, but it is true, and it is worth mentioning, just in passing, that the posture of the patient for a mirror examination is much more important than many realize.

The patient must sit well back on the seat of the chair, and then bring the chin well forward, phonating "E" as his tongue is well drawn out of the mouth, and it is amazing how many larynxes that are impossible to see if the patient slumps in the chair and pulls his chin in, will be visualized by this technic. Pardon me for describing that simple procedure before the Section. I am sure that most members of the Section can see the larynx as well with the mirror as I can. I would not presume to suggest to Dr. Equen, from what he was able to tell us about this case, a procedure to follow in the treatment. I should have to have a few more facts in hand before I could prescribe treatment for this particular case.

Dr. Taquino asked about the incision. We like the cartilage incision to be in the midline, and so far as the soft tissues are concerned, we like to do that to the side less involved in the anterior commissure cases. In the cases where we clip through, we clip the cartilage and soft tissues at the same time and in the midline. In the anterior commissure cases we also go through the cartilage in the midline, but the soft tissue and the perichondrium are incised toward the less involved side.

In regard to the Chairman's question about sulfanilamide, I do not remember a case in which we have used it thus far in the treatment of postoperative wound infection, but it certainly would be one of the first things of which to think in dealing with such a condition.

EPITHELIAL PLAQUES OF THE CONJUNCTIVA*

By J. W. JERVEY, JR., M.D.
Greenville, South Carolina

Paraphrasing Mr. Roosevelt's requirements for a good speech, we might say that the prerequisites for an acceptable scientific article are truthfulness and brevity followed by silence. In presenting these cases of epithelial plaques of the conjunctiva, I will be brief and soon quiet, remembering that

"The reason why the ancients did not readily give utterance to their words was because they feared lest their deeds should not come up to them."

Justification for this report lies in the infrequency of the condition, relatively few cases having been described, and the fact that both cases were observed within a few weeks of each other.

CASE REPORTS

Case 1.—H. H., a woman, aged 24, a beautician, was first seen February 2, 1939. About two months before coming in she received a mild burn on the right eye from an electrical contrivance being used in the beauty shop. After this she noticed a "blister" on the eyeball. The eye gradually became more and more painful. She had a slight compound hyperopic astigmatic error, for which glasses were prescribed, but never procured. The growth on her right eyeball was observed at her first visit, but because there were no inflammatory changes it was not thought responsible for her symptoms. She continued to be annoyed by pain as of a sharp foreign body in the eye. The tumor was situated on the conjunctiva of the right eye about 6 mm. from the limbus at 9:00 o'clock and measured about 1 x 2 mm. It was white, flat, granular, sessile, and was freely movable. On March 14, 1939, it was removed with complete relief of symptoms and with uneventful recovery.

Interesting and unusual features of the case were not appreciated at the time and no photograph was made, although a pathologic report was secured. The slide itself was lost through my own carelessness. The microscopic report by Dr. T. R. W. Wilson is as follows:

"Sections show a stratified squamous epithelium covering a dense connective tissue base. There is no invasion through the base line which is intact. The surface is somewhat keratotic. It appears that this is a small papillary growth and is benign."

Case 2.—E. H. S., a man, aged 30 years, unemployed, was first seen April 22, 1939. He had a moderate hyperopia with symptoms for which glasses were prescribed and relief obtained. It was incidentally observed that he had a small, flat, white, granular, sessile tumor at

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Fig. 1
Epithelial plaque of the conjunctiva showing small ovoid tumor measuring 1 x 2 mm., one-third of which is on the cornea.

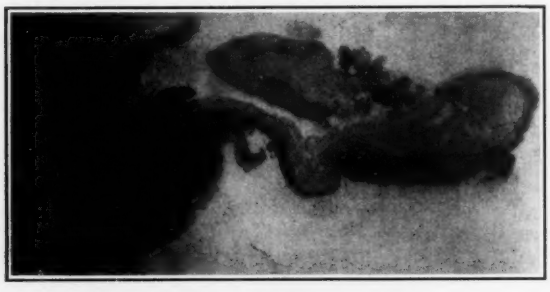

Fig. 2
Low powered section of the epithelial plaque of the conjunctiva showing greatly thickened epithelium with hyperkeratosis.

9:00 o'clock at the limbus of the right eye. This measured 1 x 2 mm., about one-third of which was on the cornea, where it was firmly fixed. The area over the conjunctiva was movable. The tumor caused no symptoms and had been present for as long as he could remember. Because of the bare possibility of its becoming malignant it was removed September 28, 1940. Recovery has been uneventful. No other pathologic condition was observed in the eye. Sections were prepared by Dr. T. R. W. Wilson and seen by Col. J. E. Ash,[2] of the Army Medical Museum. His report in part is as follows:

"The section shows an area of epidermoid metaplasia with considerable keratinization and there is in addition colloid degeneration of the underlying stroma. There are several dilated vessels also that add to the tumefaction."

COMMENT

It is tempting to place this condition in the group of the leukoplakias and so reduce the number of diagnoses to be made, but, desirable as this may be, it is impossible because the pathology is not the same. In the leukoplakias there are definite inflammatory changes, whereas in epithelial plaques of the conjunctiva there is no infiltration of round cells nor is there other evidence of inflammation. Parsons is of the opinion that these tumors are dermoids, but so far as I have been able to find out, in no case have other abnormalities been noted in these eyes, nor have there been such skin elements present as to lead to such a conclusion. It is generally agreed that specific disease is not a factor.[5]

Nicholl's[4] classification of these lesions into (1) those associated with xerosis, (2) those of congenital origin, and (3) those associated with some form of chronic irritation seems a very good one and might be expanded by omitting the word "chronic" to include the first case here described which appears to have been the direct result of a mild injury.

These tumors, especially the ones at the limbus, should be removed, because this is easily accomplished and because, while the danger of malignancy is slight, it is nevertheless present.

Grateful appreciation is expressed for the kind help of Dr. T. R. W. Wilson, of the Greenville General Hospital, and Lt. Col. J. E. Ash, of the Army Medical Museum, in the preparation of tissues and reporting of microscopic pathology. For the clinical photograph I am indebted to Dr. Hugh Smith and Mr. Roger S. Huntington, of Greenville.

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DISCUSSION (*Abstract*)

Dr. Ralph O. Rychener, Memphis, Tenn.—Despite Duke Elder's statement that "cornification of the conjunctiva is a rare pathological change which occurs in various forms," Dr. Jervey, by the report of two cases seen within three months, has cited evidence to the effect that this condition is by no means infrequent. With this opinion I am in entire accord, for epithelial plaques of the conjunctiva are quite common in our practice where the rule is to attach little significance to them unless the lesion appears to be undergoing malignant change or the patient is apprehensive because of the physical appearance or is conscious of a feeling

of foreign body in the eye. In such cases our treatment of choice is ablation by surgical excision with repair of the defect by conjunctivoplasty.

To Dr. Jervey's case reports I wish to add a third in which the excised material was examined microscopically. Miss G. E., aged 46, a teacher, was seen by Dr. E. C. Ellett May 1, 1937, because of some slight change in appearance of both eyeballs. The right eye particularly showed a flat, movable, fatty looking plaque of the conjunctiva adjacent to the limbus externally. A smaller plaque of similar appearance was situated near the limbus mesially and others were in similar positions on the left globe. No treatment seemed indicated at this time. On August 25 she returned, stating that there was an occasional feeling of something in her eyes and she had become quite apprehensive due to the yellowish appearance of the lesions which had created considerable comment among her friends. The lesions were roughly triangular with the limbus as the base, the outer ones measuring 3 x 6 mm., the inner 3 x 3 mm. The surfaces were flat and covered plaques of yellow, mulberry-like nodules of lymphangiectasis. There was no evidence of any inflammatory reactions about any of the lesions and the conjunctival surfaces did not stain with fluorescein. A clinical diagnosis was made of lymphangiectasis with hyaline degeneration and removal was advised if the patient was worried enough about them to consider this procedure. Placebo treatment was given, as the patient's family objected to surgical removal. However, on September 7 she returned of her own accord for operation and the four lesions were excised and the V-shaped defects covered by sliding the conjunctiva over them and closing with interrupted Kalt sutures, the limbal one including the sclera. Healing was uneventful and the end result quite satisfactory.

The microscopic examination disclosed that these lesions consisted of tissue surfaced by squamous epithelium of irregular thickness on which cornification was evident due to deposition of keratohyaline in the cells. Thin-walled blood vessels were present in the epithelium. There was a tendency for the processes of the horny cells to extend downward into the underlying epithelium. Degenerative changes of a hyaline nature had taken place in the submucosa where, within the stroma, there was a marked edema, no excess of capillaries, but a large area showing lipo-hyaline deposits. The lymphatic vessels were markedly distended. The diagnosis established by Capt. Elbert DeCoursey at the Army Medical Museum was: epithelial plaque of the bulbar conjunctiva and lymphangiectasis with hyaline degeneration.

The clinical significance of such lesions lies in the possibility that some few of them definitely do undergo changes closely related to tumor formation. It has been the fortune of but few men to observe the progress of an epithelioma of the conjunctiva from its incipiency to the stage where the diagnosis can be made clinically, as most patients with epibulbar epitheliomata do not come for observation until the tumor formation is well established. Therefore it behooves us to give more than a passing glance to the irritated pingueculae about which we are frequently consulted and to examine carefully the lesions discussed by Dr. Jervey.

SUCROSE NEPHROSIS AND OTHER TYPES OF RENAL TUBULAR INJURIES*

By W. A. D. ANDERSON, M.D.
St. Louis, Missouri

Sucrose has recently been added to the long list of chemical substances which may cause renal tubular damage.[1] Muller[2 3] is credited with suggesting the term "nephrosis" for the purely degenerative conditions of the kidney, meaning, presumably, the tubular nephropathies and not the degenerative vascular changes. Despite controversies over the use of this term, it seems established in medical nomenclature, and serves a useful purpose. One condition in which tubular degeneration is a prominent feature, the so-called "lipoid nephrosis," seems fairly well established as a distinctive disease entity.[4] The remainder of the nephroses is the result of poisons of metabolic, bacterial or chemical origin. The addition of sucrose to the list of chemical agents capable of producing nephrosis is of interest, not only because of the popularity of sucrose within recent years as a therapeutic agent, but also because the tubular change seems of peculiar and distinctive nature and appearance.[1] The tubular lesion, unless of mild degree, is easily recognizable, having an appearance quite different from the more familiar types of nephrosis, and may be termed a hydropic or vacuolar degeneration.

This effect of sucrose was first noted by Helmholz[5] in 1933. He described the effects upon the kidneys of rabbits which followed the injection of hypertonic solutions of sucrose, and also described the lesion in a human case. Since that time hypertonic sucrose has been used with increasing frequency as a therapeutic agent. It has been recommended, not only to lower the cerebrospinal fluid pressure[6 7 8] in cases of traumatic injury to the nervous system, but also to relieve cerebral symptoms and complications in arteriosclerotic hypertension[9 10] and as a diuretic.[9 11 12 13 14] If used in small amounts, and in properly selected cases with adequate renal function, there is no evidence that sucrose will have a harmful result.[1 15] However, the dele-

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*From the Department of Pathology, St. Louis University School of Medicine, and the Pathological Institute, University of Tennessee College of Medicine.

terious effects of hypertonic sucrose when used in large amounts, or in the presence of inadequate renal functional reserve, has been confirmed by the experimental work and published cases of several authors.[1 5 12 15 16 17] It is intended here to report two more cases exhibiting this lesion, but with certain unusual features, and to make comparisons with some other types of tubular degeneration.

Case 1.—M. R., a negro girl 15 years of age, was brought to the hospital in the eighth month of pregnancy, in labor and comatose. She had had no medical attention during her pregnancy and planned to be delivered by a midwife. Edema of the feet and ankles had been present for four months, and for three weeks she had complained of severe headaches and periods of blindness and vertigo. The night previous to hospital admission she had repeated convulsions. The urine was at low specific gravity and contained 3+ albumin. The nonprotein nitrogen content of the blood was 26 mg. per 100 c. c. She delivered a stillborn baby shortly after admission, and following delivery the urinary output was very small. For its diuretic effect, and because of the cerebral symptoms, sucrose was administered on the two days following delivery, a total of 2,100 c. c. of a 25 per cent solution being given in seven periods of injection. The urinary output was somewhat increased, but a good diuretic effect was not ob-

Fig. 1

Kidney, *Case 1.* The diffuse, widespread nature of involvement of convoluted tubules is evident. The swelling, paleness, fine reticulation and vacuolation of the tubular cells are the characteristic features.

Fig. 2

Kidney, *Case 1.* High power view of convoluted tubules, showing the fine vacuolation and droplets in lumens. In some of the swollen epithelial cells no nucleus is visible.

Fig. 3

Kidney, *Case 1.* Photomicrograph of convoluted tubules showing details of the fine reticulation and vacuolation.

tained. Infection developed, her condition deteriorated, and she died on the ninth day after delivery. Three hundred c. c. of 25 per cent sucrose were given the day before and the day of death. It is estimated that about 10 grams of sucrose per kilogram of body weight were given during the nine-day period.

Autopsy confirmed the presence of severe puerperal infection, including isolation of a non-hemolytic streptococcus and Staphylococcus aureus from the blood stream. Though the liver did not show lesions perfectly typical of eclampsia, some necrosis was found. The findings of particular interest were the renal lesions. The kidneys were large, each weighing 225 grams, and were pale and soft.

Sections of the kidneys showed an extreme degree of hydropic swelling and vacuolation involving all convoluted tubules of the cortex. These tubules, with their greatly swollen, pale staining cells, appeared in sharp contrast to the deeply staining glomeruli and medullary tubules. The swollen epithelial cells almost or completely occluded the lumen in many cases. The nuclei were not distended or swollen, but in many cells no nucleus was visible. The cytoplasm of these pale cells had a foamy, finely reticulated and vacuolated appearance, but was not water-clear, as in the cells of a hypernephroma. Small round globules frequently occupied the cytoplasm of the tubular cells, the lumen of the tubules, and the capsular spaces of the glomeruli. Neither fat nor glycogen could be demonstrated by special stains. Another and apparently independent change was seen in a few tubules in the form of hyaline droplets accumulated in the portions of the epithelial cells adjacent to the tubular lumens. Staining by azo-carmine resulted in clear differentiation of these droplets, and also indicated some thickening of the glomerular basement membrane. It seems likely that these changes are related to the eclamptic condition which was present.

Case 2.—M. J., a negro woman, aged 60 years, complained of a sudden sharp pain in the region of the right temple. Later, she was found in an unconscious condition and brought to the hospital. Her blood pressure was 200 systolic and 120 diastolic. The urine contained 4+ albumin. She was given intravenously a single injection of 250 c. c. of a 25 per cent solution of sucrose. Death occurred eleven hours later. Necropsy showed generalized and renal arteriosclerosis with cardiac hypertrophy. Cerebral hemorrhage into the right internal capsule with secondary rupture into the ventricles had occurred.

The kidneys had some fine granularity of their outer surface and were pale and soft. Microscopic examination of the renal tissue revealed a fairly severe degree of sclerosis of arterioles and small arteries with a patchy fibrosis affecting some glomeruli and regions of interstitial tissue. Almost all of the convoluted tubules were involved by a variable but usually marked degree of swelling and vacuolation. The lining of some tubules seemed so swollen as to block the lumen. The epithelial cells showed fine reticulation of their cytoplasm, or small clear vacuoles. The inner margins of the cells were ragged and irregular. Many of the epithelial cells had no visible nucleus. Red blood cells were sickle-shaped.

COMMENT

It has already been shown by experimental studies and reports of several cases that this peculiar type of vacuolar nephrosis is the result of injection of sucrose.[1 5 12 15] The first of the cases presented here illustrates the severity of the change which may result from sucrose administration and the uniform, widespread nature of the involvement of the convoluted tubules. The second case shows the marked degree of change which occurs after a single injection into an adult of as little as 250 c. c. of a 25 per cent solution. It may be noted that in both cases the kidneys were the seat of the other pathologic changes. In one case, there were glomerular and tubular lesions apparently associated with pregnancy toxemia, and in the other case severe vascular lesions were present. In several other cases which have been previously described[1] sucrose nephrosis was found to be severe in kidneys involved by marked vascular disease. It may well be that interference with renal circulation by vascular change, or a similar effect produced by thickening of glomerular basement membrane, will markedly enhance the damaging effects of sucrose. Particularly if there was a reduction in filtration rate, it would operate to prolong the exposure of the epithelial cells to the sucrose in the filtrate. Further circulatory embarrassment may have been produced in the second case by the sickle-shaped red cells. These associated disturbances in the functional condi-

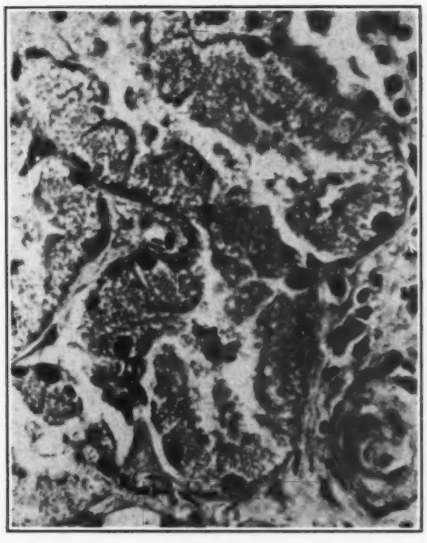

Fig. 4

Kidney, *Case 2.* Convoluted tubules showing marked degree of vacuolar change. A sclerotic arteriole is also evident.

tion of the kidney may explain the definite effects produced in *Case 2*, although the amount of sucrose administered was only about 1 gram per kg. of body weight.

There are several other points of interest and importance regarding this lesion. One of these is the nature of the change in the tubular cells. The swelling and vacuolation are apparently not associated with the presence of lipid or glycogen in the cytoplasm. Whether or not sucrose is present in the cells is not known, though the fact that there may be some slight tubular reabsorption of sucrose would suggest that this is not unlikely. The failure to stain the material in the vacuoles by any of the usual methods, and the resemblance of mild degrees of the change to cloudy swelling, in which there is known to be increased imbibition of water into the cell,[18] suggests that the change is probably a true hydropic degeneration. While some slight tubular reabsorption of sucrose may occur normally,[19] presumably by the dextrose reabsorption mechanism, Richards[20] has demonstrated that the effect of certain drugs injurious to the renal tubules is to cause greatly increased tubular reabsorption, to an extent that urinary output is greatly diminished. Experimentally, Helmholz[12 16] has been able to produce a great lowering of urinary output or definite anuria by injection of large amounts of sucrose. It may be that convoluted tubular cells are injured by contact with sucrose in glomerular filtrate to an extent that marked absorption of sucrose and fluid may occur.

The effect of the tubular changes on renal function is of practical importance. Increased imbibition of water is not necessarily very damaging to cells, and may be a reversible change, particularly if it is due to injury by exposure to anisotonic solutions.[21 22] That there is at least a temporary effect on renal function seems probable from the extent of tubular damage which may occur. This is borne out by the experimental work of Helmholz and Bollman,[12] who were able to produce a lowering of phenolsulphonphthalein excretion, and even definite anuria by injection of sucrose into rabbits. It seems equally plain, however, that little or no permanent damage results. But since temporary interference with renal functional efficiency may be of serious degree, the use of sucrose seems unwise where there is already renal damage and decrease of functional reserve.

The specificity of the hydropic degeneration resulting from sucrose also needs consideration. Klemperer[17] states that dextrose in very high

Fig. 5

Kidney from a case of poisoning by diethylene glycol. The hydropic degeneration is evident in the swollen tubular cells with the water-clear cytoplasm.

Fig. 6

Kidney from a case of enterocolitis with diarrhea in a child, the pale, swollen tubular cells showing a change similar to the damage caused by sucrose.

(50 per cent) concentration also produces vacuolation, though not so striking as the result of sucrose. Helmholz and Bollman[12] found that following injections of sodium sulfate, urea, dextrose and sorbital, similar changes were produced, but these were definitely less marked than those produced by sucrose. Hydropic degeneration has also been described as occurring in cases of chronic dysentery[23] and in poisoning by diethylene glycol.[24 25]

As a comparative study, and in a search for lesions similar to sucrose nephrosis, three groups of cases were examined. In the first group were 380 cases showing tubular degenerative changes, picked from a series of 3,000 autopsies. Among these cases none was found which might be confused with the well-developed sucrose nephrosis. Some having the more severe degrees of cloudy swelling and fatty degeneration of the tubules resembled the milder changes in tubules after sucrose administration. Some of these cases had been given dextrose. Also in one case of diabetes mellitus an appearance suggestive of mild sucrose nephrosis was present. It may probably be attributed to some slight accumulation of glycogen in convoluted tubules.

The hydropic degeneration in the kidney which results from poisoning by diethylene glycol was compared in four cases of death from administration of "elixir of sulphanilamide"! In one of these cases the tubular changes were quite mild, resembling cloudy swelling. In another the tubular damage was very severe, with necrosis and desquamation of lining epithelium. The remaining cases showed focal areas in which there was marked swelling and distortion of the lining cells of convoluted tubules. The cells had a water-clear cytoplasm, without the fine reticulation and formation of small droplets as seen in sucrose nephrosis. These differences, combined with the patchy distribution, produced a picture quite different from that of sucrose nephrosis.

The sections of kidney tissue from thirty-five cases of enterocolitis with diarrhea revealed an instance in which the renal changes appeared similar to those resulting from sucrose. The cells of the convoluted tubules were similarly swollen and had fine reticulation of their cytoplasm, but were not quite so pale staining as the cells affected by sucrose, and the vacuolation was not so marked. The change, however, was practically indistinguishable from that due to sucrose.

SUMMARY

(1) Sucrose may be added to the list of chemicals which produce tubular degenerative changes or nephrosis.

(2) Sucrose nephrosis is a peculiar type of hydropic or vacuolar degeneration affecting convoluted tubules.

(3) The probability is discussed that pre-existing renal lesions may enhance the effects of sucrose on the tubules so that changes are produced from relatively small amounts.

(4) The lesion produced by sucrose is compared with certain other types of renal tubular damage.

(5) The occurrence of a tubular lesion of similar appearance in some cases of diarrhea or chronic dysentery is confirmed.

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DISCUSSION (*Abstract*)

Dr. Robert A. Moore, St. Louis, Mo.—Last February, at the Barnes Hospital, we had an opportunity to observe at autopsy the kidneys of a lead worker who came to the Hospital with the signs and symptoms of uremia, and died some forty-eight hours after admission. At autopsy the appearance of the kidney was much as Dr. Anderson has shown. Some of the tubules in the cortex showed a peculiar hydropic degeneration.

I must confess that this slide was on my desk for some days, and finally we wrote as the diagnosis "hydropic degeneration of the renal tubules." Some time after that, Dr. Anderson's first excellent article on this subject appeared in the *Journal of the American Medical Association*. We immediately remembered this case, secured the history from the hospital, and found that the patient had been given sucrose intravenously. Since that time we have seen one additional case at the Barnes Hospital.

Even at the time that we originally studied this case we were impressed with the fact that the change occurred in some tubules and not in other tubules. The pathologic change, hydropic degeneration, was present in nodules throughout the renal substance. These nodules correspond to the nodules of tubular hypertrophy or dilatation seen in cases of chronic renal disease.

That raises the point Dr. Anderson has touched upon, which seems to me to be important. That is, what is the nature of the pathologic change? How much physiologic disturbance occurs as a result of the hydropic degeneration? Here in this kidney there is, I believe, some evidence that the change is severe and practically restricted to that part of the renal tubule which is morphologically the best preserved.

The second case showed only slight changes. In order to gain some additional information concerning the point of whether or not this lesion occurs only in damaged kidneys, I secured through the courtesy of Dr. Paul Wheeler, pathologist in charge at St. Louis City Hospital, the sections from five kidneys of individuals who had received intravenous sucrose. These kidneys in four instances were from patients who had had a traumatic injury to the cranial cavity or to the brain and were given the sucrose as a measure of dehydration. In one case the patient had rheumatic heart disease and was given sucrose purely as an experimental procedure.

The typical pathologic change in the renal tubules was present in only two of the five cases. In one case there was a severe degree of cloudy swelling. In two cases I would consider the renal tubules essentially normal, or, if you wish, there was a slight degree of cloudy swelling, depending upon the fixation and stain used. Thus, in two cases out of five examined, it has occurred in what, so far as we can determine, was a previously normal kidney in young persons injured in automobile accidents and given the sucrose as a treatment for edema of the brain. In the two cases at Barnes Hospital it occurred in previously damaged kidneys.

However, on the basis of the observations on the first case at the Barnes Hospital, I am convinced, as Dr. Anderson is, that there may be some severe damage to the kidney as a result of intravenous administration of sucrose, and one should use it sparingly in cases with renal damage. On the basis of the other observations, it would appear to be a safe therapeutic measure if there is no previous renal damage, and if it is used in young individuals. However, there should be additional studies on this point.

I should like to ask Dr. Anderson if he has made any observation concerning renal functions in individuals who have received sucrose intravenously.

Dr. R. H. Rigdon, Memphis, Tenn.—I have been very much interested in this renal lesion for approximately a year and a half now. In my experience it has occurred only in those cases in which sucrose has been given.

In the first case under consideration here, we have a complicated problem. We have three separate factors to consider. One is the bacterial infection. Second, the patient had eclampsia. The correlation of clinical eclampsia with the pathologic changes, of course, presents a problem. A third factor is that the patient received sucrose.

This lesion which has been shown certainly is neither the lesion that we see in bacterial infections, nor that resulting from bacterial toxins. It is not the lesion that occurs in eclampsia. I am speaking now of the diffused tubular change. The focal areas that were called to your attention as colloidal degeneration in the epithelial cells of the tubules would suggest a closer relationship to the bacterial infection than to eclampsia. Although this case is complicated by a bacterial infection, it is obvious that the most diffuse lesion results from the sucrose. There are other cases reported in which there are no bacterial infection that show exactly the same renal change.

Dr. Cardwell and I, at the University of Tennessee, are studying the sucrose problem both in man and in experimental animals. We made a very serious mistake in our early work, and that was in bringing the data before our hospital staff about a year ago. They quit using sucrose. Since that time we have not been able to get any cases to study at autopsy. I learned my lesson at this time about accumulating pathologic data. We are now selecting cases and giving 250 c. c. of a 25 per cent sucrose solution and checking their nonprotein nitrogen.

We were unable to find any evidence of retention of nonprotein nitrogen in two of the cases we have studied. In one case we did get retention of nonprotein nitrogen. This brings up the question of the association of this lesion with other pathologic changes in the kidney, and also why do we get a retention of nonprotein nitrogen in some cases and not in others?

Our experimental observations have been few up to this time, but we have been impressed by one point, and that is the association of dehydration of the rabbit with the production of this renal lesion. Going back to

the eight or nine cases that Dr. Anderson has reported, we find that the majority of the cases were comatose at the time of admission. We have no indication as to whether or not they were dehydrated, but it is likely, I think, that if they were comatose their fluid intake may have been restricted for a period of time. There may be some correlation between dehydration at the time the sucrose was given and the occurrence of this renal lesion. Time only can tell whether this is true. Our experimental animals are being carried with this dehydration in mind.

The association of this tubular lesion with previous renal damage seems to be open to question. In some of these cases I cannot convince myself that there was a pathologic change present in the kidney before the patient was given sucrose. I am of the opinion that this lesion is not necessarily associated with previous renal damage. It may be, but more cases must be studied to determine the relation of this tubular lesion to previous renal damage.

We must always be on guard for new lesions developing as a result of therapeutic agents.

Dr. Wiley D. Forbus, Durham, N. C.—Last year during the meeting of the Southern Medical Association in Memphis, I had the opportunity of seeing the lesions which Dr. Anderson has shown us today. With that preliminary view of the lesion in mind, I have watched carefully for changes in the kidney in the routine autopsies of our department during the past year. In this material we have seen the lesion on two or three occasions. On one occasion we found that the entire tubular structure of the kidney was involved. This, of course, is in striking contrast to the observation of Dr. Moore, who found the lesion focally distributed. This variation in distribution of the lesion suggests to me that its development may be specifically determined by the functional state of the tubular epithelium in the respective functional units. Perhaps it is to be expected that only those functional units actually in a state of activity would be apt to undergo the peculiar alteration. The same line of thought might be applicable also to the occurrence of the lesion in the injured kidney in which, as Dr. Moore has described, the lesions developed only in the areas of tubular hypertrophy and were totally absent in the injured and at least presumably non-functioning tubules.

Dr. Lucien Y. Dyrenforth, Jacksonville, Fla.—It seems to me it would be very interesting to find out what is the fate of sucrose administered intravenously. I wonder if the author can tell us anything about that.

Dr. Anderson (closing).—Regarding the effects of sucrose on renal function in man, my own observations are few. In some of the first cases I described, the nonprotein nitrogen of the blood was determined at the time of entrance into the hospital, and following administration of sucrose was greatly increased. In some instances death was due to uremia. In experimental animals, sucrose has been shown to have a definite effect on renal function.

Dr. Rigdon's comments concerning dehydration are timely and interesting. In a dehydrated individual sucrose will be more concentrated in the fluid in contact with tissue cells, with the probability of more severe injury. Sucrose is obviously a bad thing to administer to a dehydrated patient, since it will markedly increase the dehydration.

The problem of focal and diffuse changes as a result of sucrose is pertinent, particularly because of the possible effect of previous renal lesions. In the first case discussed today, the changes were diffuse, and in the second case, there was a tendency to focal involvement. It is probable that previous renal damage is an important factor determining the site of the changes.

The fate of sucrose which has been injected into the blood stream is apparently to be completely excreted by the kidneys without being metabolized. In an individual with normal renal function, the sucrose is completely excreted within twenty-four hours, and almost all within ten hours. When there is failure of renal function, the excretion of sucrose is delayed and, depending upon the degree of renal failure, it may be as long as seventy or ninety hours before urinary excretion is complete. Clearance of sucrose from the blood is similar to that of urea or creatinine, and is comparably decreased in renal disease. Sucrose does not pass the barrier of the choroid plexus into the cerebrospinal fluid. I do not know what degree of diffusion occurs into other tissues of the body.

INTUSSUSCEPTION OF THE APPENDIX*

REVIEW OF THE LITERATURE AND REPORT OF A CASE

By BARTON McSWAIN, M.D., F.A.C.S.
Paris, Tennessee

The periodic report of the occurrence of intussusception of the appendix justifies attention being called to its existence as an entity. Certain phases of its management are applicable in the treatment of the most common surgical disease of the abdomen, appendicitis. There has been no complete review of the literature on this subject since the paper of Spurney and Nyquist[1] in 1922. Such a case is being reported herewith, with a summary of the world literature.

CASE REPORT

The patient was a white man, aged 19 years, admitted to the University of Virginia Medical School Hospital July 26, 1933. He was first seen in the outpatient department on April 18, 1933, complaining of a lump at the navel. Six months before he had noticed a swelling in the right lower quadrant of the abdomen which was accompanied by severe cramp-like, intermittent pains, lasting one to two minutes and recurring at intervals of one to two minutes. The pain was relieved by self-induced vomiting. The swelling remained for a day and then disappeared, leaving residual soreness. Since

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*From the Department of Surgery and Gynecology, University of Virginia Medical School Hospital, University, Virginia.

the first attack he had had recurrent similar attacks about every two weeks, the pain being relieved by vomiting, the mass remaining for a day. There were black stools occasionally. The attack in which he was first seen began in the morning a few hours before. It was similar to those described above.

The past history was irrelevant except for a supposed appendectomy elsewhere fourteen years before.

Examination of the abdomen showed the scar of a McBurney incision and a distinct elevation in the right lower quadrant, representing a soft mass the size of a grapefruit, slightly tender on deep palpation. During the examination the mass decreased in size and at the close it could be made out only with difficulty. A benzidine test on the feces was negative.

A definite diagnosis could not be made at this time.

He reported eight days later that he had had pain every night, had been unable to retain any food, but that his bowels had moved twice daily. He had lost eight pounds. The diagnosis of partial intestinal obstruction with questionable chronic intussusception was made. Hospitalization was advised, but refused.

One week later the mass had disappeared and the patient was free from symptoms. X-ray examination showed chest, stomach and duodenum and colon normal.

Two months later he reported following another attack. There was no mass present. Three weeks later he was admitted to the hospital in an acute attack. The temperature was 99°, pulse 92, white blood count 4,800. Abdominal examination revealed a large tender mass extending from near the umbilicus in the right lower quadrant diagonally upward and to the left. There was no distention.

Exploration was advised.

First Operation.—Under spinal anesthesia a right paramedian incision was made. The ileum was intussuscepted into the colon as far as the splenic flexure. The transverse colon was tremendously dilated. The intussusception was reduced without much difficulty. Attached to the cecum in the normal position of the appendix was a dilated and thickened structure one and a half centimeters in diameter and four centimeters long, evidently the base of the appendix. On the distal end of this structure was the remainder of the appendix about two centimeters long. The distal end was intussuscepted into the proximal end (*Fig. 1*).

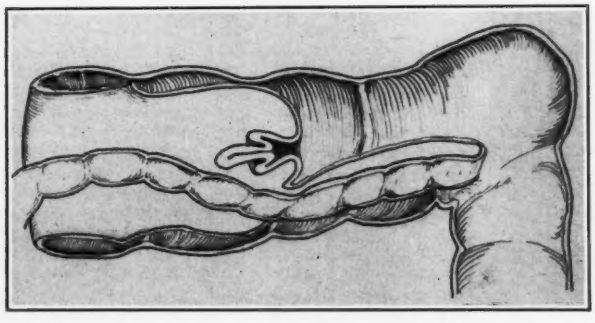

Fig. 1

Sketch showing distal portion of appendix intussuscepted into proximal portion, with accompanying ileocecal intussusception. Designated Type II, combined.

Reduction was carried out with some difficulty. The entire appendix was removed close to the cecum and the stump inverted with two purse-string sutures of silk. No other measures were deemed necessary to prevent recurrence of the intussusception because it was felt that the abnormality at the base of the appendix had been responsible for its presence. The wound was closed without drainage.

The pathologist's report follows:

"*Gross Description.*—The appendix measures 4.5 x 1.5 cm. The proximal two-thirds of the appendix is greatly swollen. The serosa is thickened and covered by reddish gray fibrin. The blood vessels are very heavily injected.

"On section the mucosa is seen to be greatly thickened, the lumen is irregular in shape and is filled with blood and pus. At the extreme tip of the appendix there is superficial ulceration of the mucosa. The lumen of the distal one-third of the appendix has been almost completely obliterated by fat and fibrous tissue.

"*Microscopic Examination.*—The lumen contains some blood, apparently traumatic. The wall is thickened and shows granulation tissue within the submucosa which is infiltrated with mixed cells.

"The diagnosis is chronic appendicitis."

The postoperative course was complicated by a transient attack of pyelitis. The patient was discharged eleven days after operation.

One month later he returned. The mass and pain had recurred two weeks after discharge. Gastro-intestinal series and barium enema, at the time the mass was present, showed no organic pathologic changes except that the cecum was well visualized and the lower ileum was somewhat dilated.

He was readmitted October 22, 1933, three months after the first operation, with pain of two days' duration, worse than ever before, nausea and vomiting, but still having normal bowel movements.

His temperature was 99.2°, pulse 72, and leukocyte count 12,600. There was very little abdominal distention or muscle spasm. Just below the umbilicus, extending completely across the abdomen, there was a slightly tender mass which intermittently increased and decreased in size. Peristalsis was audible. Rectal examination revealed nothing abnormal.

Second operation.—Under spinal anesthesia supplemented by nitrous-oxide-oxygen-ether, the old paramedian scar was excised down to the fascia. The abdomen was opened and adherent omentum freed from the lagre intestine. The apex of the intussusception extended past the hepatic flexure.

This was reduced with some difficulty until only about four centimeters of ileum remained intussuscepted into the colon. This was so adherent that it was impossible to reduce it (*Fig. 2*). The ascending colon was then opened. The intussusception had started at the stump of the previously extirpated appendix. The stump, with its two previously inserted purse-string sutures of silk, was cut through in an effort to reduce the intussusception. As this

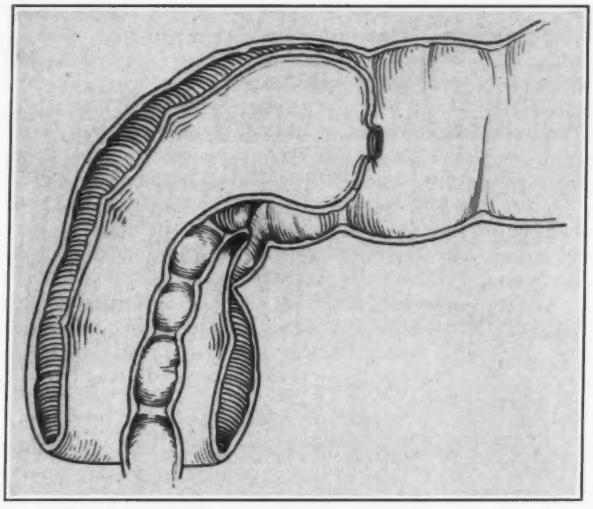

Fig. 2
Ileocecal intussusception beginning at the site of the previously extirpated appendix.

was impossible, it was necessary to resect the mass. The cecum and ascending colon being extremely mobile with a long mesentery, it was possible to deliver them upon the abdominal wall. The cecum, ascending colon and twelve centimeters of ileum were resected and the end of the ileum anastomosed to the side of the transverse colon. A Witzel ileostomy was done twelve centimeters above the anastomosis, the tube being brought out through a stab wound in the left flank. The abdomen was closed without drainage.

The pathologist's report follows:

"*Gross Description.*—The specimen consists of the cecum with the lower portion of the ascending colon and ileum attached. There is intussusception of the cecum into the colon beginning at the stump of the appendix. The ileum is invaginated into the colon at the ileocecal valve.

"*Microscopical Examination.*—The invaginated ileal and colic walls are so fused that the muscular portion of the wall of each seems fused into one with loss of serosa.

"The ileal portion shows slight necrosis of the epithelial cells of the villous type with mixed leukocytes lightly infiltrated into the underlying mucosa and submucosa.

"*Diagnosis.*—Chronic intussusception with cellulitis of the intestinal wall."

HISTORY

John McKidd,[2] of Elgin, England, in 1858, was the first to report a case of intussusception of the appendix. His patient was a white boy, aged 7, who had been having recurrent attacks of abdominal pain for one month when first seen. He was treated with calomel, castor oil, poultices and the application of leeches. He lived a month after the first examination. It was necessary to administer chloroform at intervals during the last two weeks he lived. Autopsy disclosed a completely inverted appendix, lying across but not obstructing the ileocecal valve. Roundworms were noted also.

The first report of an operation upon such a case was by Knight[3] in the *New Zealand Medical Journal* in 1890. A case of partial intussusception of the appendix with complicating ileocecal intussusception was presented. The patient, a baby of 13 months, died one hour after resection had been done.

The reports of the first cases to survive operation appeared in 1897 by Wright and Renshaw,[4] Pitts[5] and McGraw.[6]

Reference to a total of eighty-one cases has appeared in the literature. It has been possible to review seventy-seven of these and all appear to be authentic except two which are open to question.

CLINICAL MANIFESTATIONS

The youngest patient was aged 13 months. The eldest was 65. The average age was approximately 16 years with forty-three cases in the first decade, eight in the second, six in the third, four in the fourth, five in the fifth, two in the sixth and three in the seventh. The age is not given in the remainder.

There were forty-three males and twenty-eight females. The sex is not given in four.

The shortest period which had elapsed between the onset of the attack and operation was two or three hours. Only one case was treated as promptly as this and only five were operated upon within twenty-four hours. Forty-nine patients had had recurrent attacks for a variable period of time, the longest period being nine years, before coming to operation. This was not only in the early days of aseptic surgery; the patient who was referred to Christopher[7] in 1938 had been having attacks for seven years. The average duration was approximately eight months.

The pain was usually cramp-like or colicky and fairly severe. It was in most instances intermittent and paroxysmal. The paroxysm usually lasted from one-half to three minutes, sometimes ten to fifteen minutes. There was complete freedom from pain in the interim. The pain was usually generalized, but in some cases it was confined to the epigastrium or the right lower quadrant of the abdomen.

Nausea and vomiting almost universally accompanied the pain. In the majority of cases, the bowels moved normally. In eight cases, there was blood only in the stools; in four, mucus only, and in nine both blood and mucus. In only one was there absence of fecal passage. This occurred in a case accompanied by ileocolic intussusception, but in nineteen cases, including the case being reported, in which this complication had supervened, there were normal bowel movements.

There was only slight fever, increase in pulse rate or leukocytosis except in patients in whom necrosis, gangrene or peritonitis had occurred. Distention was mentioned in only three cases of simple intussusception of the appendix and in only six cases of the combined type. A palpable mass was noted in forty-three patients. Of these, seventeen were in individuals with intussusception of the appendix alone and twenty- six in patients with accompanying ileocolic intussusception. The tumor varied in size from a small, round, barely palpable one to a large, round, oval or sausage-shaped mass extending completely across the abdomen. The tumor increased and decreased in size under observation in some instances, even to complete disappearance. As a rule, there was little muscle spasm. Tenderness was not extreme and was confined to the tumor or one quadrant, usually the right lower one. Visible peristalsis was mentioned in three cases. The intussusception extended low enough to be palpated on rectal examination in six cases.

In Bishop's[8] case the mass presenting at the rectum was ligated and amputated close to the bowel, the intussusception replaced and the bowel inflated. The mass disappeared from the rectum, but the pain, vomiting and left lower quadrant mass persisted. The abdomen was opened, the intussusception reduced. In the place of the appendix there appeared its stump inverted with the ligature within the lumen of the bowel, constricting all three coats of the intestine. The patient recovered.

In Burghard's[9] case the small mass presenting at the rectum was ligated and excised. Examination showed the excised mass to be the appendix turned inside out with a papilloma from the mucous membrane at or just distal to the ileocecal orifice. Re-examination of the patient disclosed that the ileocecal valve could be felt by digital examination. The abdomen was opened and the bulk of the intussusception reduced but, as it was impossible to reduce the remainder, a resection was done. The patient died on the tenth postoperative day from "purulent bronchitis," although the abdominal condition was good.

In only one case was it an incidental finding. Evans[10] discovered it in the routine removal of the appendix after doing a salpingo-oophorectomy for pelvic inflammatory disease.

SUMMARY OF CLINICAL MANIFESTATIONS

From the foregoing one can state that intussusception of the appendix unaccompanied by ileocolic intussusception is difficult to distinguish from simple acute appendicitis. Jalaguier[11] diagnosed his third case correctly and MacLennon[12] diagnosed his second as either intussusception of the appendix or enterolith in the head of the cecum. Other preoperative diagnoses were appendicitis, intestinal obstruction, intussusception and malignancy. The following points aid in the differentiation:

(1) The history of more attacks than are usually seen in acute appendicitis.

(2) The more definitely cramp-like pains, similar to those of early intestinal obstruction.

(3) The history of blood or mucus or both in the stools or their discovery on examination.

(4) The history of palpation of a mass in the right lower quadrant.

(5) Less fever, increase in pulse rate and leukocytosis than would be expected in an individual with the appendix inflamed enough to cause a clinical picture of equal severity.

CAUSE

In seven cases, including the case being reported, it was stated that the cecum was abnormally mobile or had an unusually long mesentery. McKidd[2] thought that the roundworms present in his case aided in the formation of the lesion. However, they were recorded to have been found in only one other patient. Trinci[13] thought that vigorous muscular movements, such as occur in constipation, had some etiologic significance. Coopernail[14] suggested that lack of a meso-appendix might be responsible, but he

was the only author who reported this finding. A concretion was found at the base of the appendix in one case and a polypoid tumor in five cases. A mucocele was present in Morgan's[15] patient. A history of trauma was given in five cases. Corcoran[16] thought that the cause was an attempt to extrude a lymphoid follicle. Tuberculosis of the intestines was mentioned in two cases. Acute inflammation or gangrene was present in twenty-five cases. However, it is impossible to state whether the inflammation initiated or was secondary to the intussusception. It is obvious that a markedly inflamed, indurated appendix cannot become intussuscepted.

AUTOPSY FINDINGS AND OPERATIVE FINDINGS AND PROCEDURES

Five cases were discovered at autopsy. Two of these (if Rolleston's is accepted) were incidental in patients who had died of some other primary cause and the other three were the cause of death.

Intussusception of the appendix has been found to occur in four distinct ways. It can begin at the tip and extend as in *Fig. 3*. This will be designated Type 1. Here the tip of the appendix is the intussusceptum and its more proximal portion is the intussusception. There were only two of these.

It may begin at the base as illustrated in *Fig. 4*. The distal portion of the appendix is the intussusceptum and either the cecum (*Fig. 4-B*) or the base of the appendix (*Fig. 4-C*) is the intussuscipiens. Its formation thus will be designated Type 2. There were twenty-seven of these.

In Type 3 the proximal portion of the appendix forms the intussusceptum and is received into the distal portion. There was only one of these; the appendix was 19 centimeters long (*Fig. 5*).

The end result of either Type 1 or Type 2 is complete inversion of the appendix into the cecum (*Figs. 3* and *4*). When this is found at operation or autopsy, there is no way of knowing whether the primary process was Type 1 or Type 2.

Complete inversion following Type 3, intussusception of the proximal part of the appendix into the distal (*Fig. 5*) is impossible.

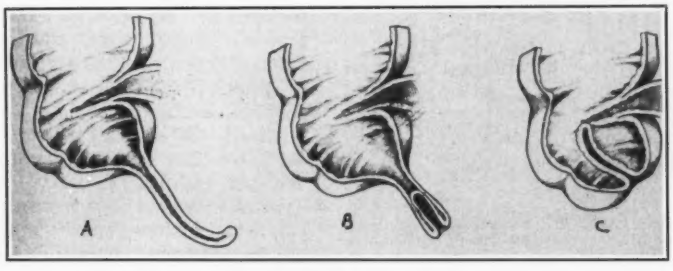

Fig. 3

(A) Normal appendix, cecum and ileocecal valve. (B) Intussusception of the appendix beginning at the distal end. The tip is the intussusceptum and the more proximal portion is the intussuscipiens. Type I. (C) Complete inversion of the appendix, Type IV. When this stage is reached, it is impossible to determine whether the process began as Type I or Type II (*Fig. 4*).

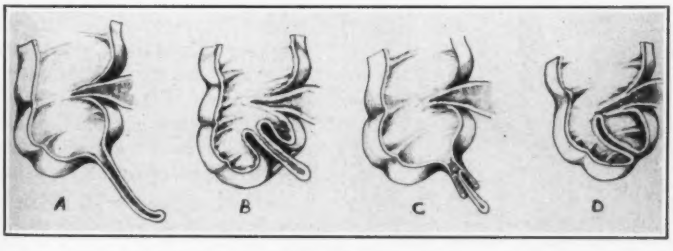

Fig. 4

(A) Normal structures. (B) Intussusception beginning at the appendicocecal junction. (C) Intussusception beginning near the base of the appendix. Both (B) and (C) are designated Type II. (D) The end result is complete inversion of the appendix.

Types 2 and 4 have been noted both alone and accompanied by the cecocolic or ileocolic or both kinds of intussusception. These will be called Types 2 combined (fourteen cases, (*Fig. 1*) and 4 combined (sixteen cases) (*Fig. 6*). The two cases of Type 1 and the one of Type 3 were unaccompanied by ileocolic intussusception.

Here the ileum may be truly intussuscepted into the cecum (three, including the case being reported) or merely dragged along (four), its relation to the ileocecal valve remaining unchanged. The discrepancy in totals throughout this review is due to lack of complete data in the original articles.

There were forty-four of the simple type, thirty of the combined type and

one in which the data were insufficient to classify it.

In intussusception beginning as ileocecal or ileo-ileal and dragging the appendix along, the normal relationship of the appendix to the cecum is not changed. There is no true intussusception or inversion of the appendix. No further discussion of this type of lesion will be made.

In cases of incomplete intussusception of the appendix, the diagnosis at laparotomy is made on sight. If reduction is possible, this is done. If any difficulty is experienced in the reduction, the operator should grasp the cecum and make firm pressure on the base of the appendix with his thumbs while his assistant exerts gentle traction on the distal end. Even when adhesions between the appendix and itself or the appendix and the cecum prevent reduction, appendectomy can usually be effected. In such instances, a cuff of cecum can be excised and closure done by inversion by purse-string with a larger defect, inversion by sutures of the Lembert or Halsted type.

When complete inversion has occurred, no appendix can be seen. The difficulty here is indicated by the fact that in three instances the patient had been operated upon previously, twice in one case, and the abdomen closed without even the finding of the appendix. (In one of these the first operation was for an ovarian cyst and the appendix might not have been sought.) These cases were explored subsequently and found to have complete inversion of the appendix. In all these cases, however, there was a dimple present at the normal site of emergence of the appendix from the cecum. In some reports, it was stated that a small portion of the meso-appendix could be identified. In several, a pencil-like structure could be felt within the cecum. In this type, reduction is rarely possible; usually a cuff of cecum must be removed by elliptical incisions and the appendix brought out along with it. Difficulty of securing closure of the cecum has been noted in only one case (Cooper[17]). Pitts[5] in a case of complete inversion made elliptical incisions, let the appendix drop into the cecum and closed the cecum. It is interesting to note that Edebohls'[18] operation for appendicitis was inversion of the appendix into the cecum without removal. The appendix was supposed to slough off and to be passed by rectum, but undoubtedy it remained more or less intact in many cases and continued to cause pain. Furniss[19] removed a microscopically normal appendix six years after it had been inverted by Edebohls' operation.

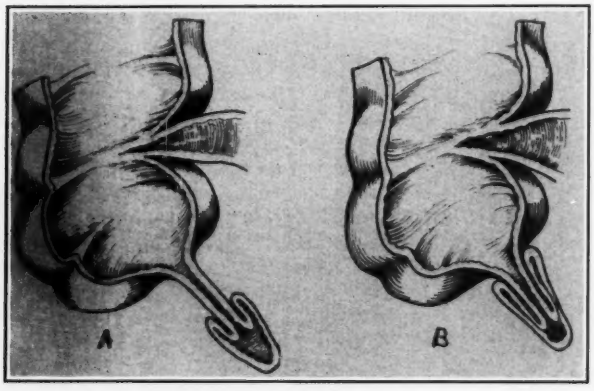

Fig. 5
The proximal portion of the appendix forming the intussusceptum and being received into the distal portion, Type III. (A) shows the initial, (B) the final stage.

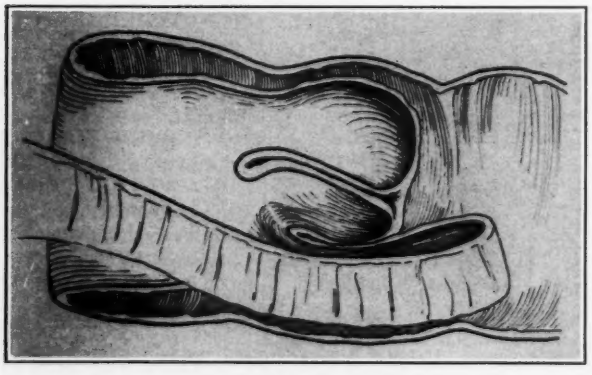

Fig. 6
Complete inversion of the appendix with accompanying ileocecal intussusception. Designated Type IV, combined.

It was necessary to resect the whole cecum in only two cases of the simple type.

When ileocolic intussusception has accompanied that of the ap-

pendix, the intussusceptum should be milked out, of course. If this is impossible, resection of the cecum and parts of the ileum and ascending colon may be necessary with restoration of continuity as the operator deems best. Resection was done in sixteen cases of the combined type.

In order to prevent recurrence of the intussusception, Wallace[20] sutured the cecum to the lateral abdominal wall after reducing an ileocolic intussusception and removing the appendix. Rogers[21] sutured the ileum in the same manner after a resection. It certainly seems to be a rational move in instances in which resection is not done.

INTUSSUSCEPTION AT THE SITE OF THE STUMP OF A PREVIOUSLY REMOVED APPENDIX

In addition to the case being reported, Roquette's[22] patient undoubtedly had intussusception at the site of the stump of a previously removed appendix. His case was a boy, aged 4 years and 10 months, with ordinary ileocolic intussusception which was reduced, the appendix removed and the stump inverted with two purse-string sutures of silk. Nine days later he began vomiting and passed nothing by rectum. Twelve days postoperatively he presented a mass in the epigastrium, had paroxysms of pain and passed blood by rectum. At the second operation the apex of the intussusception was felt at the splenic flexure. It was reduced almost completely when the cecal wall gave way and a polypoid mass (the appendix stump) started through the rent. The cecum with three inches of colon and two inches of ileum was resected and anastomosis done. The patient recovered. The specimen showed the swollen, inflamed polypoid stump of the appendix with two ligatures under a dimple in the cecum, which had been the starting point of the intussusception. Two cases are reported by MacLennon,[23] but it is not clear whether these were cases of true intussusception beginning at the stump or merely stump appendicitis.

RESULTS

Five cases were found at autopsy, seventy at operation. Sixty cases recovered, five died. Of the fatal cases, one was simple intussusception of the appendix, with death due to pulmonary embolism; four were accompanied by ileocolic intussusception.

Excepting the case being reported, no recurrences have been recorded. Roquette's[22] case cannot be considered a recurrence because, although it was an ileocolic intussusception beginning at the site of a previously removed appendix, it was not originally an intussusception of the appendix.

In my case, intussusception of the appendix was accompanied by ileocolic intussusception. After reduction and removal of the appendix, ileocolic intussusception occurred at the site of the stump of the previously removed appendix.

Intussusception of the appendix is classified as Type 1, beginning at the tip; Type 2, at the base; Type 3, proximal portion into distal portion; and Type 4, complete inversion. Types 2 and 4 have been described both alone and accompanied by ileocolic intussusception.

The mortality of intussusception of the appendix alone was 2.6 per cent, of intussusception of the appendix plus ileocolic intussusception was 14.8 per cent and the total mortality 7.7 per cent.

CONCLUSIONS

(1) The typical case of intussusception of the appendix occurs in a child under ten with a history of numerous attacks of severe cramp-like abdominal pain with complete freedom from symptoms in the interim, a small palpable mass in the right lower quadrant of the abdomen, very slight elevation of temperature, increase in pulse rate or white blood count and a small quantity of blood and mucus in the stools.

(2) This lesion is probably more frequent than this number of cases indicates and is probably present in patients who have been explored, but in whom the appendix is not found.

(3) The inverted stump of an appendix has been the starting point of an intussusception in at least two cases. This fact should make one seriously consider the advice of Horsley[24] against inversion of the stump; or at least one should be careful to leave as short a stump as possible.

(4) In a patient who continues to complain of pain after a supposed appendectomy, one should consider the possibility that the appendix may not have been removed or that an intussusception at the site of the stump of the appendix may be present.

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DISCUSSION (*Abstract*)

Dr. George Johnson, Nashville, Tenn.—If one finds a case of intussuscepted appendix, I think it would be well not to try to reduce the appendix. As Dr. McSwain said, it had been done in some cases. In some cases it was impossible and the appendix had to be excised. Certainly his own case and possibly one other that had a second intussusception of the stump would lead one to believe that the tendency is there, and if so it would be much better, if he discovered the case, even if reduction could be carried out successfully, completely to excise the appendix, leaving no mass to start a secondary intussusception.

The fact also that two of these cases were recurrences and the other case primarily from a stump, brings up the point again of whether or not it is best to invert stumps of appendices. Certainly they do not lead very frequently to intussusception or we all would have seen them. On the other hand, many men have advocated not turning in the stump, and certainly we have operated upon a great many appendices where that was difficult and we have not done it, and no untoward results have occurred.

The most interesting thing about this paper is the possibility of diagnosis before operation, which might be rather important. The clinical picture is very similar, except for the history of many attacks, to what we know as acute appendicular obstruction or obstructive appendicitis, as contrasted with the ordinary inflammatory type. The clinical picture of that was very well described by the late Dr. Wilkie, of Edinburgh, and it has always been a fascinating thing to try to differentiate that type of acute appendicitis preoperatively from the other type.

Clinically, with the exception of the passage of blood and mucus in the stools, which occurs in any intussusception, these patients exhibit the same type of clinical picture; that is, severe cramping pain, pain out of all proportion to the general illness of the patient, with lowered white count and fever. In addition to that, of course, if they have an intussusception they have a mass in the right lower quadrant.

Ordinarily when we see a patient with the signs and symptoms of appendicitis and find a mass in the right lower quadrant, we immediately think that they have an appendical abscess, that they have had a ruptured appendix which has been walled off, and the consensus of opinion usually is that operation should be delayed in those patients. Certainly operation should not be delayed, however, in the presence of intussusception, and it may well be a rather important thing to try to determine by the symptoms whether some of these patients with the finding of a mass may have intussusception, in which case they should be operated upon.

Dr. Hugh A. Gamble, Greenville, Miss.—The question always arises as to what brings about an intussusception. We are told by our textbooks that it is usually irregular peristalsis. Sometimes a foreign body or new growth causes it, but none of the theories has ever gone very deeply into the subject. Personally, I feel that there is a very lucid explanation for practically all cases of intussusception. I once saw an intussusception take place. A patient had come in for an intestinal obstruction. I opened his abdomen and found an intussusception of the ileum into the ileum. This was reduced, and shortly afterward I noticed a rapid peristaltic wave coming down the ileum. It struck a quiescent part of the bowel and telescoped itself into it and went on down for about four inches.

I feel that the speed and the force with which a peristaltic wave travels has a great deal to do with whether an intussusception will occur or not.

Another thing is whether it strikes a quiescent part or fixed point. Thirdly, difference in size plays a significant role. That is one reason why we often find an intussusception at the cecum, ileocecal intussusception. A rapid wave travels down the bowel; it strikes the large fixed bowel with a difference in the diameter of the lumen, and an intussusception results.

Another thing is the difference in type of motion of the peristalsis of the small bowel and the cecum. The cecum has more of a churning motion, while that in the small bowel is progressive in character, and if it is of sufficient force and rapidity, can push right on into the large bowel. To a certain extent I think that is what happened in these cases.

I went over the reports of quite a number of cases that have been found, and a number of patients reported that they had small tumors at the base of the appendix. Two of them particularly reported that the base of the appendix was large, and one or two reported that they had a narrow meso-appendix. What I think really happens there is that peristalsis occurs in the appendix just as much as in any other part of the intestinal tract, and if there is an opening large enough to allow the appendix to telescope into itself, it will go right on in.

The second question that arises is how to prevent it. There is a very simple measure, which we have used for years, in the prevention of intussusception in children. It is by anchoring the cecum with the appendix itself and suturing the space between the cecum and the abdominal wall with two catgut stitches so that there is no danger of intestinal obstruction's occurring at this point. This procedure effectively prevents a recurrence of an intussusception.

Dr. J. Murry Davis, Memphis, Tenn.—I should like to stress some of the symptoms of intussusception which are much like those of appendicitis. There is probably just a little difference, and we all like to try to make our diagnosis before we open the abdomen. First, intussusception seems to be found more fre-

quently in young people, the pains are more cramp-like in character, and there is an intermittent stage in which the patient is pain-free and seems to be all right. The muscle spasm is less than that found in acute abdominal lesions or acute abdominal appendicitis, and there is a very slight or no elevation of temperature. Some of these cases, I understand, had no fever.

The blood count is not increased as much as it often is in appendicitis. However, in many cases of appendicitis the blood count is not increased, anyway. The pulse rate is increased as found in appendicitis. Occasionally blood is found in the stools and also we occasionally find an appendix-like mass in the lower quadrant. As in some of the abdominal problems, the intussusception has to be handled by the surgeon as best suited to the findings in each individual case. After examining all the records in Memphis here, I was unable to find any true intussusception of the appendix. A large number of cases of intussusception were reported, and in a number of them the appendix was drawn in with the intussusception, but there was no true case of intussusception of the appendix into itself.

Dr. McSwain (closing).—This is not a common condition, but I think it is something that we ought to have heard of once. Many patients are operated upon and continue to have symptoms of appendicitis; both of these cases that I found that were operated upon and no appendix found were operated upon by good surgeons. The surgeons apparently did not tell the patients that the appendix was not removed, and they continued to have symptoms.

When one opens the abdomen and cannot find the appendix, he should remember that such a thing as complete inversion of the appendix occurs and that it may be possible to feel the appendix in the cecum as a pencil-like mass.

VESICOVAGINAL FISTULA*

By ERASMUS H. KLOMAN, M.D.
Baltimore, Maryland

History.—No clear reference to these distressing and at one time common disorders is found in medical archives until the latter part of the Sixteenth Century and early part of the Seventeenth, when several descriptions appeared almost simultaneously in the writings of de Mercado, a Spanish physician, Felix Plater and Severin Pineau.

Plater gives two clear pictures of the fistula following difficult childbirths, the second case being appropriately titled, "vesicae cervicis alia ruptura in partu."

H. von Roonhuysen (1663) first proposed the closure of such a fistula by suture.

J. Fatio has left an excellent account of the way in which he carried out the suggested procedure of von Roonhuysen's in 1675 and 1684 by placing his patient in the lithotomy position and exposing the fistula with a speculum. He then freshened its edges with a pair of fine scissors and brought the edges together by passing a sharpened quill through them and winding a thread over the ends of the quill to keep it in place.

A. J. Jobert de Lamballe was the first operator who systematically treated a large number of cases, many of them successfully. His plan of treatment for the simpler cases consisted in traction on the cervix so as to expose the fistula, followed by broad denudation of the edges of the fistula and their exact approximation by interrupted sutures. When the fistula was a large one, and the approximation difficult on account of the tension, he made incisions in the lateral vaginal walls parallel to the fistula so as to permit the tissue to be drawn together.

G. Seman, in 1854, did away with the lateral incisions, substituting in their place a method which still bears his name, the use of double sutures, one introduced at a distance from the wound edges for relief of tension.

J. Marion Sims, in 1852, combined the three essentials for success, the speculum, the suture and the catheter, and placed the operation at the disposal of the profession.

The discoveries to which he laid claim were these:

(1) A method by which the vagina could be distended.

(2) A suture not liable to excite inflammation or ulceration.

(3) A method of keeping the bladder empty during the process of recovery.

L. von Dittel, in 1893, made a radical departure from all precedent by opening the abdomen, detaching the bladder from the uterus, and so exposing the fistula, which he then sewed up, the sutures including only the bladder wall. The vesico-uterine peritoneum was then closed, and finally the abdomen.

A. Mackenrodt, of Berlin, in 1894, adopted a somewhat similar plan, but made a definite advance, in that he operated through the vagina and detached the bladder on all sides from the fistula. He then sewed the bladder up independently and closed the opening in the vagina by drawing its sides together.

Howard Kelly, in 1896, split the margin of

*Read in Section on Urology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

the larger fistulas posteriorly. The four steps of the operation were carried out as follows:

(1) A crescentic incision was made around the posterior two-thirds of the fistula, separating by a blunt dissection the bladder with its muscular and mucous coats from the vagina and the cervix laterally, and all the way up to the peritoneum.

(2) The remaining anterior third of the fistula was then pared on its vaginal surface, denudation being extended down to, but not including, the vesical and urethral mucosa.

(3) The ureters were marked out and protected by passing two flexible ureteral catheters 2¼ millimeters in diameter through the urethra, one into each ureter.

(4) The detached part of the bladder behind was now easily drawn forward and accurately united by interrupted fine silkworm-gut sutures to the immovable anterior third of the fistula on its vaginal surface; each suture was made to catch the under surface of the muscular wall of the bladder so as to turn its edge up into the newly formed bladder. The ureteral orifices were in this way directed upward, and they escaped compression and transfixion through the presence of the catheters. The vaginal opening was not closed.

Dr. Kelly says:

"I left the ureteral catheters in place three days to drain each kidney through the urethra, and put the bladder entirely at rest, thus avoiding any strain on the healing tissues."

All modern operative technic for the repair of urogenital fistulas is based upon the work of these pioneers.

In 1918, Rawls described his so-called "fascia lapping" technic for the cure of cystocele. Later he recommended adoption of the same procedure for the cure of vesicovaginal fistula. This operation, which requires careful, painstaking dissection of the anterior vaginal wall, was subsequently modified and simplified by Bissell. In 1939, Aldridge reported a cure in two cases from the clinic of the Woman's Hospital of New York, in which he used a modified Bissell's technic.

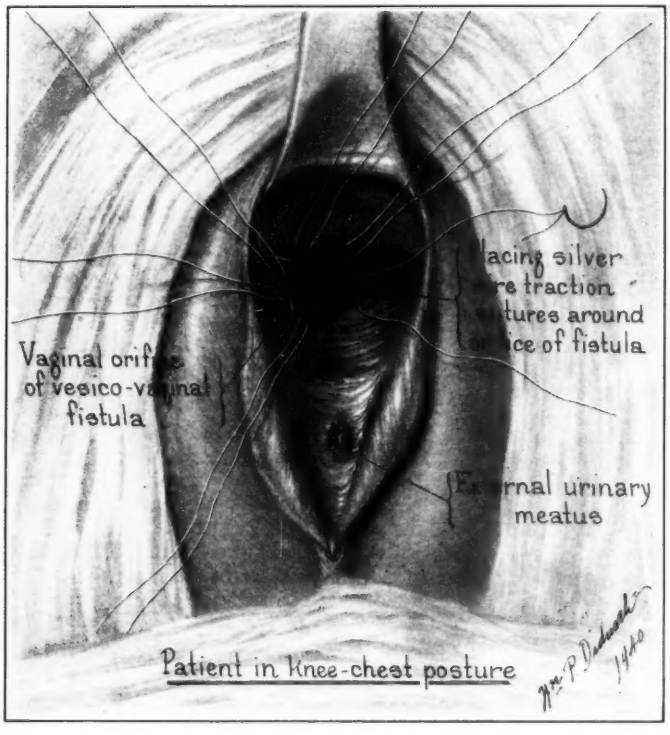

Fig. 1

This illustration shows the completion of the first step, the placing of the wire stay sutures. By gentle traction these stay sutures bring the fistula toward the vaginal orifice and make it accessible. These stay sutures are held by Halsted clamps. This is an essential step in getting good exposure.

W. C. Danforth, in April, 1940, published his article on "Transperitoneal Approach in the Management of Inaccessible Vesico-Vaginal Fistulas." His operation was similar to that reported by Legueu in 1914 and by Walters in 1937.

It must be borne in mind that the early authors and the authors up to the Twentieth Century who wrote on this subject were dealing mostly with fistulas caused by obstetrical accidents. The author has been deeply interested in this surgical problem for many years, but his efforts to cure fistulas have so far met with only a fair average of success. Present-day

fistula continues to be the cause of a great deal of worry over unsatisfactory results. We mean by "present-day fistulas" those occurringg in the wake of pelvic and vaginal operations, and especially those accompanying the use of cautery and radium. These two agents are prone to produce a fistulous opening which usually is far more inaccessible than the older obstetrical fistula. With the patient in the lithotomy position, the average obstetrical fistula is comparatively easy to expose by pulling down the cervix, whereas the present-day postoperative fistula is not only high up in the vaginal vault and almost inaccessible, but is too frequently very difficult to expose because of the presence of dense scar tissue.

Years of sympathetic contemplation of the deplorable physical and mental status of the victims of vesicovaginal fistulas and participation in the common experience of frequent failures in our surgical efforts at relief have been the two chief factors stimulating an evolutionary development of the simple but helpful technic herewith presented.

PRELIMINARY STUDY AND TREATMENT

It may not be amiss to emphasize the importance of a very thorough and accurate preliminary study of the various factors involved in determining the proper approach. The survey should include visual examination, preferably with hand-mirror and a strong light, vaginal speculum and cystoscopic examination. The latter will show the location of the bladder opening with relation to the urethral sphincter, the trigone and ureters, and the approach in the individual case will be governed by the extent of involvement of these structures. In those cases in which the ureter is found opening into the margin of the fistulous tract it will sometimes be necessary first to transplant one ureter, or both ureters, into some other portion of the bladder before proceeding with the fistula closure. Occasionally one is able to transpose the ureteral opening to a higher position in the bladder by simply splitting the ureterovesical valve for a short distance. By introducing a ureteral catheter through the Kelly cystoscope before operation, one can more easily mobilize the lower ureter during the fistula dissection, and the catheter may be retained for a few days until the edema of operation subsides. The character of the entire vesical mucosa with respect to encrusted or interstitial cystitis must be determined. Any infection of the urinary tract should be overcome if possible. The bladder urine of a patient with vesicovaginal fistula is usually sterile, but if it shows infection the upper tract should be carefully examined for evidence of ureteral stasis from stricture or other causes, and measures should be taken to restore better renal

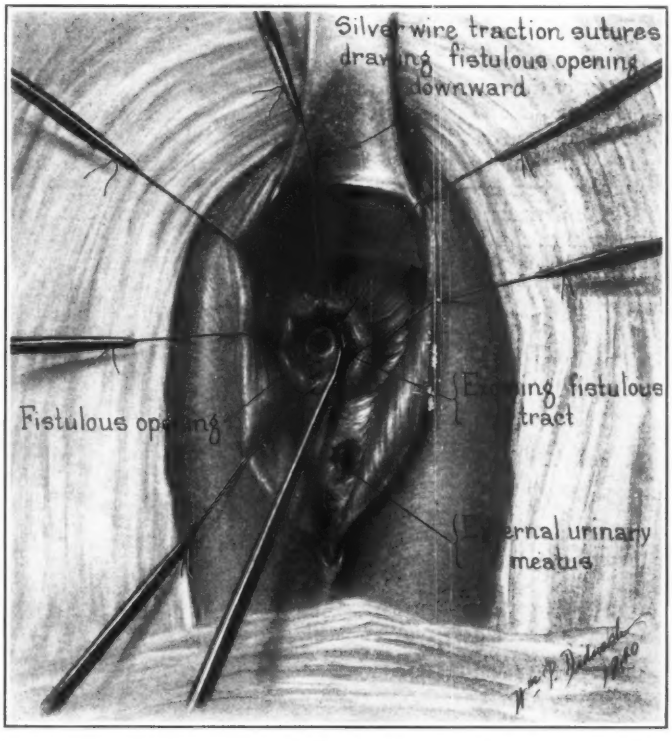

Fig. 2

In this step the fistula has been drawn down almost to the vaginal orifice. This transforms a difficult into an easy operation. This illustration also shows the beginning of the dissection around the fistula. The stay sutures immobilize the operative field throughout the entire operation.

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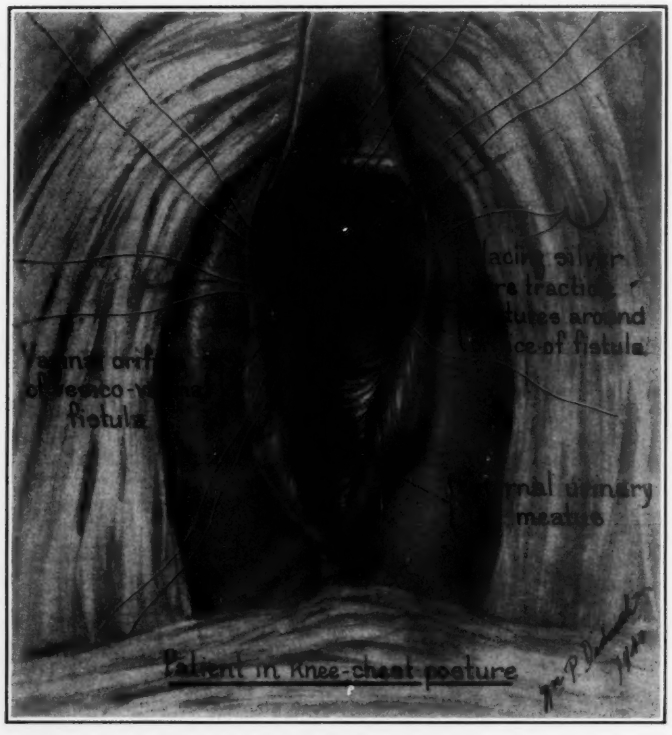

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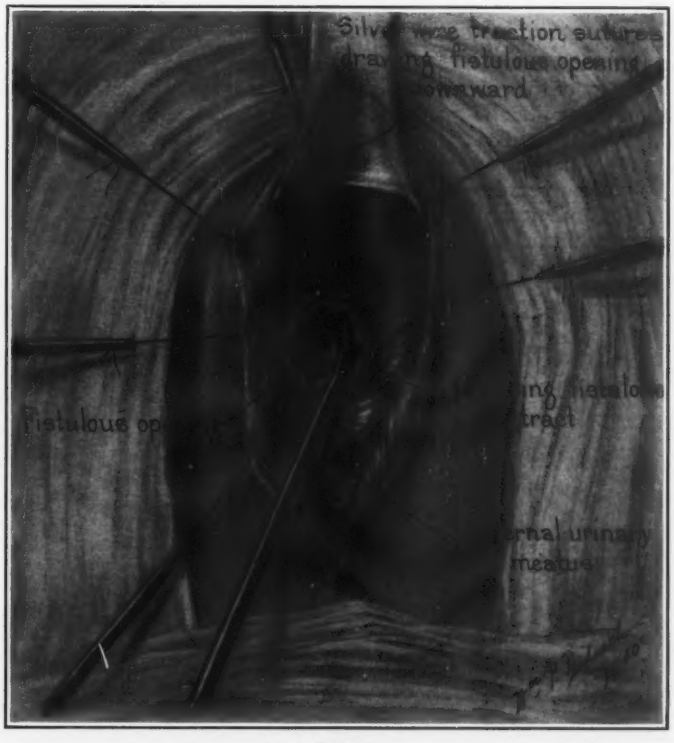

Fig. 2

In this step the fistula has been drawn down almost to the vaginal orifice. This transforms a difficult into an easy operation. This illustration also shows the beginning of the dissection around the fistula. The stay sutures immobilize the operative field throughout the entire operation.

drainage and rid the kidney of infection before attacking the fistula. If any tendency to stone formation is present, the urine should be kept acid. Preparation of the vaginal mucosa should be very thorough. We do not believe it is necessary to sterilize the vagina chemically, but we do believe it should be cleaned thoroughly with green soap and water.

Although many methods of reaching inaccessible vesicovaginal fistulas have been attempted, the author is convinced that the vaginal approach, when feasible, minimizes the shock to the patient, offers less opportunity for complication, and hence a better chance of success.

THE OUTSTANDING FEATURES IN THIS OPERATION ARE POSITION AND EXPOSURE

In our series of cases we used the knee-chest posture for operation. Better exposure is thus afforded, this being particularly true when the vaginal outlet is narrow, when the fistula is large or when the fistula is located near the vaginal vault. An added advantage of this posture lies in the fact that one is working down on the operative field rather than up to a field beneath the ramus of the pubis. With the patient in the lithotomy position, frequent sponging of blood is one of the tedious features of an operation. With the knee-chest posture, however, bleeding is less profuse because of the relative anemia of the elevated tissues, and much of the already reduced amount of blood oozes into the bladder out of the operative field. Using the special device for the operating table which we have designed, we carry the patient to surgical anesthesia in the dorsal position. She is then turned to the prone position, so that the upper portion of the symphysis rests on the lower portion of the lift, which is well padded with some material such as sponge rubber. The lift is then raised, flexing the hips and knees to the point where the patient can be placed in the knee-chest posture, then lowered slightly, until some of the weight of the body is taken by the femurs. The table-top portion rises with the lift, giving support for the trunk and shoulders of the patient.

We will not discuss the type of operation we use because, as before stated, this varies according to the character and location of the fistula and according to the preference of the individual operator. We have, however, employed a few modifications or additions which we consider noteworthy. Inasmuch as exposure of the operative field is the chief prerequisite to the success of any operation, in cases in which the fistula is high in the vaginal vault, or inaccessible, we do not hesitate first to do a perineotomy, which can easily be repaired following closure of the fistula. The next problem is to bring the fistulous opening as near the vulva as possible in order to facilitate dissecting and closure of the fistulous tract. This is effected with six to eight traction sutures of stainless steel wire, which are introduced into and through the submucosa of the vagina. These should be placed about one to two centimeters from the fistulous opening and, by means of traction on these sutures, the fistulous tract can be brought near, or in conjunction with the introitus and held there until the operation is completed. This procedure is, we believe, different from any other type of exposure yet described.

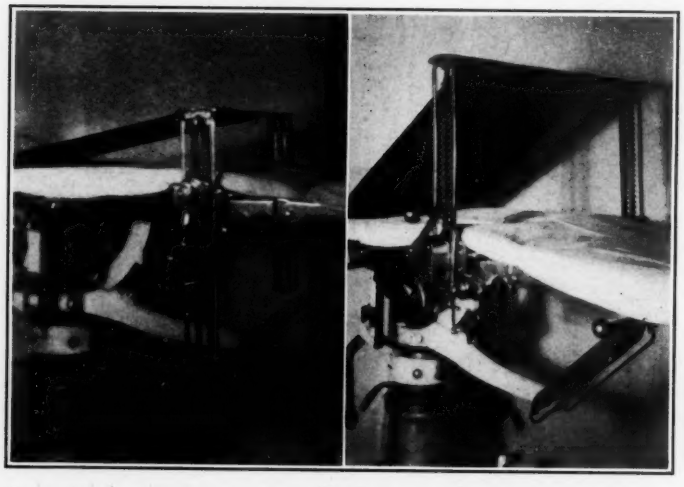

Fig. 3

The table device is adapted for any operating table and is found not only satisfactory in vesicovaginal fistula work, but also in the Kelly cystoscopy where anesthesia is required.

One of the principle requisites of any operation for closing a vesicovaginal fistula is the complete separation of the vaginal mucosa and the bladder in order to allow closure of each layer without too great tension. Wherever

possible the line of suture closing the vaginal mucosa should be at a right angle with that closing the bladder mucosa. If conditions necessitate closure of the two layers in the same direction, one should endeavor to place each of the two lines of suture on a different lateral plane.

The bladder opening is closed with catgut sutures, the first suture being usually a purse-string, which is reinforced by a second layer of continuous catgut.

For the third line of sutures concerned in the closure of the vaginal flaps, we use a non-absorbable fine dermal. In our earlier cases, we employed chromic catgut with good results, but we are now convinced of the superiority of a non-absorbable suture. Silver wire and stainless steel wire are advocated by some surgeons, but in our experience these metals have exhibited a greater tendency to cut through the tissues and to produce more discomfort than the softer, pliable type material. The theory behind the use of a non-absorbable suture here is that there is less danger of infection's being carried in from the vaginal vault along the suture line.

POSTOPERATIVE TREATMENT

Practically all writers agree that the essential factors of the postoperative treatment of vesicovaginal fistula operations are rest or comparative immobilization of the suture line and relative dryness. These objectives are attained by placing a self-retaining catheter in the urethra. Should incrustation of urine salts form on the catheter, it should be changed every three to four days, and the patient should be placed on some medication to acidify the urine. It is during this postoperative period that the resident, intern and nursing staff play a very important role. It is almost necessary to have them instructed as specialists in caring for these patients, as neglect of many apparently trivial matters may lead to poor results following what had seemed to be a very satisfactory operation. The bladder should be irrigated twice a day with some mild solution, such as boric acid, guard being kept against the injection of more than one to two ounces of fluid at a time. In our early cases the bladder was drained by the gravity method, but in our more recent cases we have found a Steidman pump for suction preferable. The catheter must be kept in the bladder for twelve to fourteen days, which allows sufficient time for the bladder and vaginal flap to heal. After removal of the catheter, the bladder should be emptied by catheterization every four to six hours, the patient gradually relearning to void.

Patients are kept in the prone position for the entire time during which the catheter is in place, as this position affords better drainage of the bladder.

We do not consider it necessary to use any vaginal douches, but we do believe the vulva should be kept clean by pitcher douches or sponging twice a day.

The suture line in the vagina is painted with some mild antiseptic solution only after the catheter is removed, and the sutures are allowed to remain in the vaginal mucosa for about four weeks.

In offering this operation we are not laying claim to originality, but are hoping rather to stimulate others to take advantage of methods that have been found to be relatively simple and far more effectual than those now generally adopted.

Since the turn of the century, Howard A. Kelly and his associates have used the knee-chest posture in operations on both the difficult and ordinary fistulas and, of course, this posture is only an exaggeration of the elevated lateral hip position recommended by Sims for work on difficult fistulas. About 1900, one of Dr. Kelly's staff men, the late Clement A. Penrose, constructed a special table for holding the fistula patient in the knee-chest posture. This proved rather complicated, however, and dependence was again placed on an assistant on either side to support the patient in the knee-chest posture.

We believe that our special table device offers the easiest method for elevation of a patient to the knee-chest posture, as well as for indefinite retention of this position.

Dr. Kelly devised the shepherd's crook, the right angle tenaculum, and other instruments for dragging the vaginal walls toward the vulva, but these traction instruments are often in the way during the dissection and final suture of the fistula, while our multiple wire retractors offer no obstruction, and they flatten out the tissues surrounding the fistula more effectively than one or two straight handled tractors.

In conclusion, the following points might be recapitulated:

(1) The importance of careful examination to determine the size and position of the fistula.

(2) Careful preoperative study and treatment, including cystoscopy, to determine the

relationship of the fistula to the ureters and urethra.

(3) Introduction of a catheter in one ureter, or both, before operation, in cases presenting close proximity to the fistulous tract.

(4) Transplantation of one ureter or both, or a splitting of the ureterovesical valve.

(5) Use of the knee-chest posture during operation.

(6) Use of steel wire sutures for traction to obtain exposure.

(7) Use of non-absorbable sutures in the vaginal vault, which remain for about four weeks.

(8) (a) Prone position as long as the catheter is in place.

(b) Self-retaining catheter with constant suction for twelve to fourteen days.

(c) Maintenance of urine on the "just acid" side to help prevent urinary deposits on the catheter and line of sutures.

44 W. Biddle Street

DISCUSSION (*Abstract*)

Dr. Horatio N. Dorman, Washington, D. C.—As I understand it, Dr. Kloman closes the mucous membrane in the vagina and he obtains a perfect result. We cannot get that.

In July of 1939, Dr. Ertaugh, of Oak Park, described a method of treatment of some of these cases in the *Urologist's Review*. At that time we had a case that we had tried twice unsuccessfully to close. Dr. Ertaugh's operation looked very rational and simple enough, so we tried it in our case that was in trouble.

The operation was done through the vagina. A cystoscope was passed, a urethral catheter into the cystoscope and into the tract, and then a urethral catheter was threaded through that. An opening was made through it and into the fistulous tract.

Dr. Ertaugh makes a large, round incision, making a cuff one centimeter long, and this cuff he folds up onto his catheter and sews on. We used a catheter that was a little too large to come through the opening, so this point just stopped at the mucous membrane of the vagina and we sewed it there with four sutures, one each north, east, south and west. Incidentally, with the catheter in place, and urethral catheter, if this catheter will not come through, you have a beautiful retractor. You do not need to use the suture with this brought up and sewed in the four places. This is returned into the vagina.

You have really a water-tight closing and the catheter is left in for drainage.

Dr. Kloman did not bring out something that seems to me to be very important, namely: the closure of the musculature between the layer of bladder and the vagina. That seems to me to be the most important part of the whole operation and in this operation, after this is drawn back into the bladder, two or three sutures are placed around this tract.

Traction is used, they are drawn together moderately tightly, and that gives you a fairly strong layer of musculature between the bladder and vagina.

We put three sutures in our case. It was our third attempt and we did not want to miss it.

In the after-treatment of these cases an important point was brought out by the late Dr. Clute, of Boston, to wit: placing the patients on the abdomen while they heal up. That gives you a dry field to heal, and I think it is a help.

The catheter sloughed out in our case on the eleventh day and we used another catheter for a few days to be absolutely sure that the girl made a perfect recovery. This operation was done last summer and I think it is well worth-while.

Dr. Kloman (closing).—Dr. Dorman's case is entirely different from these which I have shown you. His is what we call the old type, the cases following obstetrical accidents that are comparatively rare now. The cases that I have just shown you are what I speak of as the present day type of vesicovaginal fistula, usually resulting from some form of operation such as complete hysterectomy, the use of radium, or the use of cautery. Where these are followed by fistulous openings, there is no cervix or uterus to help pull the bladder down into the outlet. In fact, they are usually so far up in the apex of the vagina and held there so tightly by scar tissue that it is very difficult to expose the fistulous opening. It is comparatively easy to repair the cases following obstetrical accidents where the uterus and cervix are intact, and by traction the cervix can be pulled down, resulting in good exposure. We do not use the knee-chest posture in repairing this type of case.

Dr. Dorman's operation for the old type case should be very satisfactory and I can easily see why he should get good results. I agree with him that there is a great deal of muscle between the vagina and bladder that can and should be brought together in making such a repair, whereas in the present day type the entire septum is very much thinner and you usually have difficulty in separating the vaginal mucous membrane from the bladder. However, we always try to close all the dead space, and if we find any muscle we always use an extra row of sutures to close this space.

In regard to the position of the patient postoperatively, I question that putting them on the abdomen has much, if anything, to do with the ultimate result. I have been working over these cases for thirty years and have tried it on a great many. My feeling now is that if I place them on the back where they are comparatively comfortable and they keep the bladder empty with the use of a Steidman pump, the possibility of getting a good result is really better than by trying to keep the patient on the abdomen. We allow her to move from side to side and find that the patient's attitude is much better and she is much more cooperative. The patients seem to enjoy taking care of the Steidman pump, leaving it on for three-quarters of an hour and then turning it off for one-quarter of an hour.

EARLY SIGNS, SYMPTOMS AND DIAGNOSIS OF PROSTATIC OBSTRUCTIONS*

By I. G. DUNCAN, B.S., M.D., F.A.C.S.†
Memphis, Tennessee

Hypertrophy of the prostate is a disease of middle and old age, rarely occurring before the age of 45. However, congenital bars, valves and contractures may be found at a much earlier age.

Some of the etiologic factors are chronic infections, sexual irregularities such as masturbation, abstinence and excessive petting and congenital anomalies.

The prostate consists of five lobes: anterior, posterior, median, and two lateral. Hypertrophy may take place in any one or more of these lobes. Excessive fibrous tissue growing across the vesical neck is known as a bar. The enlargement may be due to an excess of either the glandular or the interstitial connective tissue. Congenital lesions consist of constrictions at the vesical neck, prostatic valves, and so on.

The signs and symptoms of prostatic obstruction may be divided into two classes: (a) local and (b) general or constitutional.

(a) LOCAL SIGNS AND SYMPTOMS

(1) *Nocturia.*—Nocturia is often the very first symptom. The patient seems to void about as usual during the day, but will have to get up several times during the night. This is especially true upon the onset of chilly weather, and is more noticeable during the early morning hours. As the disease progresses, the nocturia increases until it reaches a stage where it is most annoying and the patient is getting very little sleep.

(2) *Dribbling.*—At the end of urination the last few drops are expelled with such little force that the clothing is likely to be soiled, and this is often referred to as the "rubber boot" stage.

(3) *Dysuria.*—Dysuria or difficulty in voiding may be a troublesome symptom, and especially so if the bladder has been allowed to become overdistended.

(4) *Diuria.*—As the disease progresses and the bladder becomes involved, diuria develops. Not infrequently this is the symptom which brings the patient to the physician.

(5) The bladder muscles become weak and lose their tone as the obstruction is increased. This makes voiding more difficult and a chronic retention is the result. This residual urine is irritating to the bladder, predisposing to an infection. If this occurs, all of the above symptoms are aggravated.

(6) In the early stages of prostatic obstruction, the urine may show very little abnormality, only an occasional pus cell, with possibly a trace of albumin. The specific gravity will usually be low, and this is very significant. However, after an infection has developed, much pus and blood may be found. This bleeding may be only microscopic in amount, or it may be so profuse that the bladder will be filled with clots. In atypical cases, severe bleeding may be the first symptom.

(7) If the residual urine is large in amount, an overflow is likely to take place, resulting in bed-wetting.

(8) In due time, if the proper treatment is not instituted, an acute retention will occur.

(b) GENERAL OR CONSTITUTIONAL SIGNS AND SYMPTOMS

The general constitutional signs and symptoms of prostatic hypertrophy are: backache, weakness in the legs, shortness of breath, dizziness, hypertension, insomnia, heart lesions and nephritis. All of these conditions may be associated with or directly caused by disease of the prostate.

Some of the more common complications are: pyelitis, pyelonephritis, stones in the bladder, epididymitis, diverticula and uremia.

Pyelonephritis is caused when the infection in the prostate and in the bladder reaches the kidneys, whether by direct extension up the ureter (which becomes dilated by back pressure), or through the lymphatics. It is a very serious complication, as the back pressure plus the infection may rapidly damage the kidneys. This in turn overworks the heart, resulting in a myocardial insufficiency. This is likely to result in a chronic uremia with an accompanying increase in the blood chemistry. Dizziness, hypertension, shortness of breath, indigestion and abdominal distention are often merely manifestations of the trouble caused by prostatic obstruction.

If stones are found in the bladder, the prostate should be suspected. The straining incident to

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†Associate Professor of Urology, University of Tennessee College of Medicine.

voiding may cause the bladder wall to give way, thereby forming small pockets known as cellules, or even a diverticulum may result.

Epididymitis results from an associated vesiculitis, the pus being forced down through the vas into the epididymis.

DIAGNOSIS

The above history will be very suggestive. A rectal examination should be made and the size, contour and consistency of the prostate noted. If the gland is found to be fixed, indurated, irregular and nodular, a malignancy should be suspected. Occasionally stones in the prostate may be confusing, but their presence can be readily demonstrated by an x-ray picture, or by the passing of a metal instrument or a sound.

If, however, the prostate is normal to palpation, this does not rule out vesical neck obstruction which may be caused by a bar, a contracture or by an enlarged median lobe. Remember, these forms of vesical neck obstruction cannot be detected by rectal examination. The patient should be examined for residual urine, and if there is as much as 200 c. c. he should be slowly decompressed. It is a very dangerous procedure to empty too rapidly a chronically distended bladder. A cystogram is of great value. The exact amount of prostatic protrusion into the bladder can be definitely shown, and at the same time diverticula, irregularities and filling defects will not be overlooked. I wish to call your attention to the air or pneumocystogram. It has the same diagnostic value as those made with the usual pyelographic media, and in addition stones can be seen. Furthermore, the air cystogram is painless and it is much less expensive.

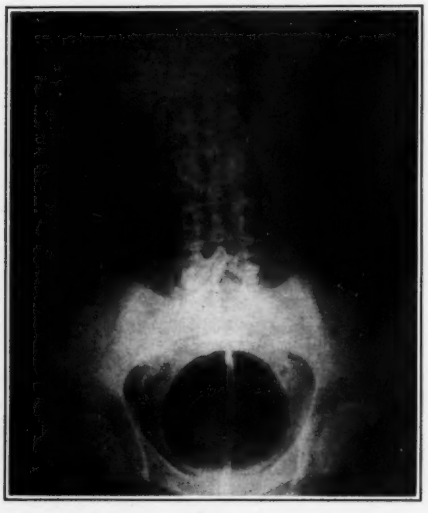

Fig. 1
Pneumocystogram showing enlarged prostate protruding into the bladder.

A cysto-urethral examination with a pan endoscope will show the proportion of the prostate protruding into the bladder, the size of the lateral lobes, and the extent to which they fall into the urethra. This is also one of the best methods for determining the type of operation best suited for the removal of the obstruction in certain individual cases. Strictures of the urethra which have many symptoms in common with prostatic obstruction can also be diagnosed, or ruled out, by this procedure. Hence, I suggest that a cysto-urethroscopic examination be made in all cases where feasible.

TREATMENT

For convenience the treatment may be divided into (1) palliative; (2) preoperative; (3) operative; and (4) postoperative. These steps will be taken up individually in the order named.

Palliative treatment is used in early cases. The general health should be improved by regulating the patient's habits, hours and diet and by giving him iron, vitamins and other tonics. Diuretics and urinary antiseptics such as alkalies, urotropin, sulfanilamide and methylene blue should be administered as indicated. If the patient is anemic or has a hypertension, sulfanilamide should be given very guardedly.

The local treatment should consist of prostatic massage every four to seven days, dilatations and bladder irrigations. The latter are best given by means of a catheter. Weekly injections of the male hormones (testosterone propionate from 10 to 25 mg.), in our hands have been very helpful. Most of these patients are going through the change of life, as women do, and are greatly benefited by male hormones. They feel better, are not nearly so nervous, and are capable of doing more and better work, mentally and physically. The patient voids more easily and the nocturia is markedly reduced. As the above outlined treatment usually causes the prostate to stop growing, or even to become smaller, many sufferers can be carried very comfortably over a period of years.

INDICATIONS FOR RADICAL TREATMENT

(1) Cases which do not improve under the above outlined plan of treatment, especially where nocturia is a prominent symptom, even though no residual urine is present.

(2) When two ounces or more of residual urine are found, and relief is not obtained by treatment and catheter drainage. Men with more than 60 c. c. of residual urine will rarely be permanently relieved without surgery, and they should be operated upon without undue delay.

(3) Patients who have had attacks of acute retention of urine should always have the obstruction removed at the earliest possible time.

(4) Enlarged prostates which tend to bleed should receive immediate attention, and a biopsy should be made to determine whether or not a malignancy is present.

PREOPERATIVE CARE

If four ounces or more of urine are present, the bladder must be drained by an indwelling catheter. The catheter should not be too large (16 to 18 mm.) and it should be changed every four to five days. If much infection is present and it is not controlled by catheter drainage, or if the patient be intolerant to the catheter, a suprapubic cystotomy is advisable, even though the obstruction is later removed by a resection.

Large stones in the bladder had best be removed by suprapubic cystotomy and the bladder drained before the prostate is removed. However, small stones, where the prostate is not too large and the infection is mild, may be taken care of by a litholapaxy.

We recommend a routine vas ligation and prefer that it be done at least several days before, rather than at the time of operation, as advised by some. In weak and anemic old men, blood transfusions have been most satisfactory in our hands.

Before a patient is considered ready for an operation the following conditions must have been met: (1) he must have had sufficient drainage; (2) his general condition must be good; (3) his blood nitrogen must be low and his phenolsulfonephthalein high; (4) his heart must be in good condition and his blood pressure satisfactory; (5) he should have a feeling of well-being and should be "anxious to go."

CHOICE OF OPERATION

Formerly, all of these prostates were removed either by suprapubic cystotomy or by the perineal route. Then, transurethral resection held the spotlight. However, our experience has shown us that when we have a big adenomatous prostate with large lateral lobes which tend to fall into the posterior urethra, a prostatectomy is preferable to a resection. At the present time we are resecting about 85 per cent of our cases.

In suitable cases, transurethral resections have the following advantages over prostatectomies: (1) a much lower mortality; (2) poorer risks can be operated upon; (3) the time of hospitalization is only about one-third of that from prostatectomies; (4) the sexual power is not affected; (5) patients do not seem to dread a resection so much as a prostatectomy. However, the after-care following a resection is a little more tedious than that of a prostatectomy, and recurrences take place about twice as often.

AFTER TREATMENT

Removing the obstruction does not cure these old men. It only puts them in a position to get well. Many of them have severe bladder and kidney infections as well as crippled hearts. Hence, they should be under the care of their physicians for some months, preferably for the balance of their lives. Their bladders should be irrigated until the infection is under control. The vesical neck should also be dilated at regular intervals for some months to prevent the formation of a stricture or a contracture. Their hearts should be kept tuned up and tonics and urinary antiseptics should be administered as required.

I wish to call your attention to the use of testosterone propionate in these old men. The use of 25 mg. weekly has given us very happy results.* Our mortality rate has been markedly reduced by beginning its use immediately after operation, or even before, where possible.

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*"Oreton," 25 mg., was supplied us by the Schering Corporation for clinical trial. I wish to thank them for their courtesy and cooperation.

Paper of Dr. Duncan is one of three composing a Symposium on Prostatic Hypertrophy. The other two papers and the discussion will appear in a later issue.

THE EVOLUTION OF THE X-RAY TUBE*

By FRANK E. HOECKER, PH.D.
Kansas City, Missouri

The story of Roentgen's "accidental" discovery of x-rays during some simple experiments with the gaseous discharge tubes of Leonard and Crookes is one of the classics of modern science. It is the purest of speculation to inquire as to whether x-rays would ever have been discovered if the tubes had not already been at hand. It is probably just as futile to question whether Roentgen or anyone else would have used discharge tubes as a spring board for the development of an instrument to aid medical science in its struggles with injuries and diseases of humanity. Fortunately, the discharge tubes were at that time standard equipment in every well-equipped physics laboratory and were consequently widely available to the medical profession when Roentgen announced that they were the source of rays which would penetrate objects opaque to ordinary light. Brought from their academic seclusion by the amazing discovery, these laboratory curiosities became the prototype of the x-ray tube. Innumerable developments and alterations followed in rapid succession as physicians and physicists sought the ideal tube.

In the year 1904, approximately eight years after the discovery of x-rays, Dr. Charles W. Allen, of the New York Post Graduate School of Medicine, in his treatise, "Radiotherapy and Phototherapy," gave the following description of the ideal x-ray tube. It is one, he said,

"(1) that will preserve a constant vacuum;

"(2) that will run for an indefinite length of time without overheating;

"(3) in which the rays will emanate from a single geometric point;

"(4) in which the angle of greatest intensity of radiation of the rays will be such as to render these rays available in the direction of greatest convenience without interference from other parts of the tube;

"(5) in which the material of the tube will not be fluorescent to the rays and thus insure freedom from one element of false light;

"(6) that is composed of a material which does not absorb any of the rays;

"(7) that is imperishable during any length of service."

When one considers how closely he approached a description of the modern x-ray tube, it may appear that he possessed a sort of clairvoyance. No doubt his extensive experience and comprehension of x-ray problems did endow him with unusual sagacity. Yet one has but to recall that Dr. Allen and his contemporaries were struggling with the early form of the now obsolete "gas tube." Specification of ideal characteristics required only the enumeration of those qualities which the gas tube did not have.

Dr. Allen could have included a characteristic possessed by modern tubes, but as yet undreamed of in his day, namely: the ability of the tube to produce any desired quality of x-rays entirely independently of and coincidentally with any desired quantity. Perhaps he may have considered this entirely too much to ask for.

When one remembers the extensive ramifications in space of these old tubes, the multitudinous variations in form, size and structural detail, the mergence of bulb into bulb through the medium of simple and compound curve, one need not wonder at the early radiologist's prayer for something simple. Perhaps I should confess that my interest in x-ray tube development embodies certain elements of esthetic appreciation of these bulbiform examples of the glass blower's art. My collection of 25 or 30 of these curvacious specimens may be merely an expression of the well-known masculine susceptibility to the beauty of curve.

Nor is such a collection entirely without physical interest.

Physically, an x-ray tube is an instrument which converts electrical energy, that is, a stream of electrical charges moving with extremely high velocity in a partial or complete vacuum, into x-ray energy. This occurs when the moving charges, often called cathode rays, strike a fixed object. In the earliest gas tube, the one Roentgen used when he discovered x-rays, the charges were given off by a flat disk of metal enclosed in a partially evacuated glass bulb, and they produced x-rays when they struck the walls of the bulb.

Although there are records[1] of the use of just such a bulb by physicians and physicists for emergency radiography of the hand or other thin bodily parts, the picture was very fuzzy and blurred due to the large size of the source of x-rays. This was remedied by using a concave cathode which focussed the cathode rays to a point. But the intense heat generated by such

*Read in Section on Radiology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

a concentration melted the glass wall where the electrons struck and ruined the tube. To avoid this, a piece of metal, usually a very thin disk of platinum, was mounted inside the tube and the electron stream was focussed on this. This led to the discovery that the quantity of x-rays emitted by a given stream of electrons was vastly greater when they struck a metal target or anode. In fact, the intensity of x-ray emission depended very greatly upon which metal was used.

These methods of increasing detail in roentgenograms and increasing intensity of emission encouraged physicians to attempt other uses of x-rays such as roentgenography of the chest and abdomen, not to mention therapy, feats hopelessly beyond the earliest tube, in fact actually beyond the capacities of available tubes when the attempts were first made. Platinum targets melted, glass bulbs punctured, gas pressure changed capriciously and often disastrously. Be it to the everlasting credit of the pioneer radiologists, both present and past, that they have always pushed their tubes to the limit, and beyond, in their attempts to conquer the problems of disease.

Tube failures and other difficulties met in extending the realm of radiology brought the physician and physicist into ever closer cooperation. The physician pointed out what a tube had to do; the physicist has found the solution of how to build a tube that would do it.

Melted targets, blackened and punctured tube walls, excessive cost of platinum brought many tentative solutions. Always there was sought the happy balance between the physical properties of available materials and the ideally desirable properties, high melting point, high thermal conductivity, low volatility, low cost, and high efficiency of emission. No substance possesses these in the desired degree, but one can compromise. Tungsten has the highest melting point of any metal, and possesses the other qualities to a fair degree. Combined with tungsten as the target material have been various methods of cooling; a tungsten block imbedded in a massive copper block for distribution of generated heat, conduction of heat outside of tube through a massive copper bar attached to the target, water cooling, oil cooling, cooling of a solid tungsten target run at a bright red heat by radiation, and rotation of the tungsten target. All of these methods[2] have been tried at various times, often discarded and tried again to be brought finally to approach perfection.*

The gas in the early tubes was a necessary evil. Indispensable to the formation of the cathode ray stream, yet completely undependable and almost uncontrollable, it was the bane of the radiologist's existence. The necessity of adjusting the gas pressure in accordance with the quality and quantity of x-rays needed for any particular job, led many a radiologist in desperation to maintain a separate tube for each of his radiological needs, a sort of radiological harem as it were. Yet even that was no solution, for in a sense it only multiplied the troubles. The gas pressure in a tube changed with use, and worse yet without use. Some means of adjusting the pressure was an essential part of every tube. An attempt to describe all the various methods employed for regulating gas pressure would become an essay in itself. A few examples will suffice for the purposes of this discussion.

The gas regulator was usually attached to the

*For example, the first rotating anode tube was built in 1897.

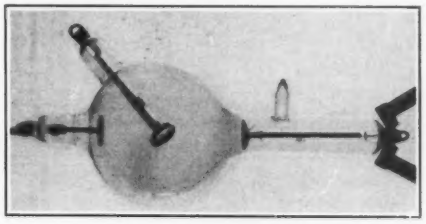

Fig. 1

Date: 1897. Notable features: prominent anode opposite a concave cathode; thin platinum disk target supported in a shallow, base-metal cup by crimping; absence of pressure regulating device; small size.

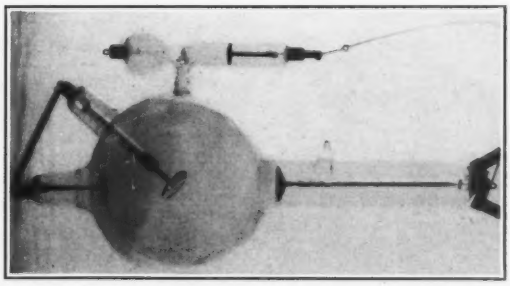

Fig. 2

Date: 1900 to 1908. Notable features: solid disk target; pressure regulation devices, left hand bulb for decreasing pressure, right hand bulb for increasing pressure, both accomplished by electrical discharge.

main bulb through a side tube. The favorite and simplest method of increasing gas pressure (the pressure was usually decreased by use) was to seal into the side tube a quantity of asbestos or other material which would give off gas when heated. The desired increased pressure was obtained by passing an electric spark through the substance to heat it. Another method was to utilize the osmotic properties of platinum or palladium. These metals permit hydrogen gas to diffuse through them when they are heated to redness. A small tube, closed at one end, of one of these metals was sealed into the x-ray bulb wall. The passage of hydrogen gas into the bulb was obtained when the osmosis tube was heated by a gas flame. Perhaps the most elegant tube of all made use of two of these osmotic adjusters. Pure hydrogen gas at a low pressure was contained in the main bulb to which were sealed two small auxiliary bulbs. One was completely closed and contained hydrogen gas at a pressure higher than that in the main bulb. Hydrogen gas flowed from it into the main bulb through an osmotic regulator connecting the two when the regulator was heated by an electric spark. The other auxiliary bulb was open to the air so that hydrogen gas passed from the main bulb to the outside through the platinum tube when it was heated in the same manner.

It is easy to see that no gas tube was ever really satisfactory due, of course, to the presence of the gas. The riddle confronting physicists was, how to get rid of the gas without at the same time eliminating the essence of the x-ray generation process, the electron stream.

The solution of the problem is another example of the strange and unexpected ways in which the problems of one scientist may be solved by the apparently unrelated discoveries of another. The discovery, although made by Edison in 1883, was first put to practical use by Fleming in 1905, when he built the first radio tube. He made use of the fact that electrons are evaporated from the surface of a metal when it is heated to a high temperature. In 1913,

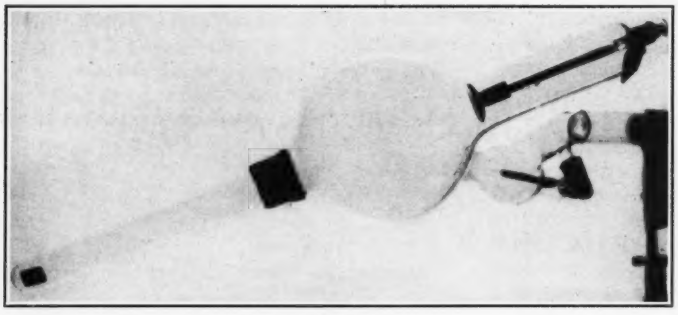

Fig. 3

Caldwell Cavity Tube. Date: 1903. Notable features: small, electrically isolated target at extreme end of long tubular extension which was inserted into body cavity; anode withdrawn into side bulb near cathode; glass handle for supporting tube in any desired position.

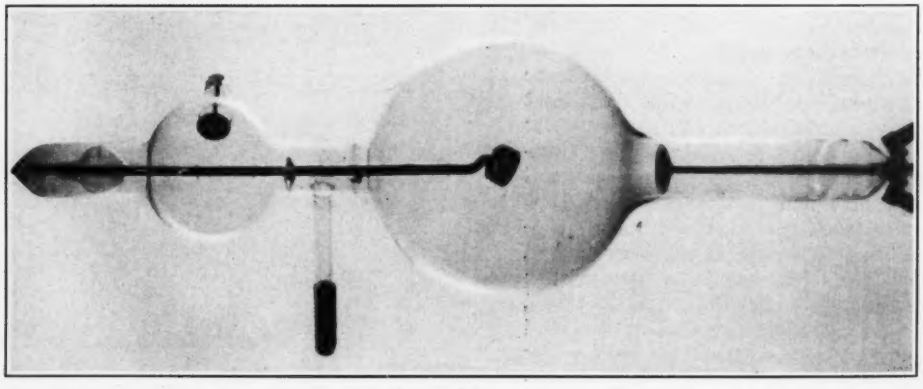

Fig. 4

Double Bulb, Voltohm Tube. Date: 1906. Notable features: heavy tungsten block target; anode located in auxiliary bulb far from target; absence of pressure regulating devices.

Coolidge applied this to the x-ray tube by replacing the concave cathode of the gas tube by a metallic filament which could be heated by an electric current passed through it. The electrons furnished by the heated wire took the place of the electrons which had been furnished by the gas in the tube and he could now evacuate it completely so far as vacuum technic would permit. And with the gas went all the problems owing their existence to its presence.

It should not for a moment be supposed that the design or form of all tubes previous to the advent of the Coolidge tube had been conditioned entirely by the exigencies mentioned above. There had been many adaptations based upon the particular usage for which the tube was intended and upon the source of the high voltage. An instance of this was the cavity tube of Caldwell built in 1903. This tube had its target located in the end of a long thin tube attached to the main bulb. When this long tube was inserted into a body cavity the source of x-rays was very close to the tissue to be treated. Yet such adaptations were definitely subject to the limitations of the gas tube. One of these was, of course, that the tube must be readily accessible for regulation of the gas pressure. Flexibility in usage and mounting were greatly hindered by the many protruding bulbs and other excrescences.

With the advent of the Coolidge tube these limitations were banished and designers were free to begin a multitude of special adaptations for specific purposes.

The search for the ideal tube has ended with the realization that it was nothing more than

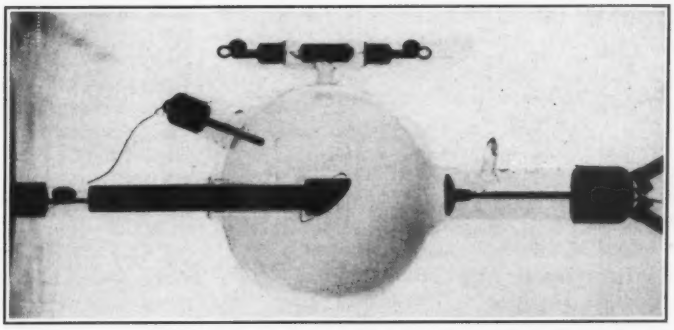

Fig. 5

Date: 1910. Notable features: tungsten target embedded in massive copper block; target enclosed in glass shield; pressure regulating device for increasing pressure through the heating by an electric current of a gas emitting substance.

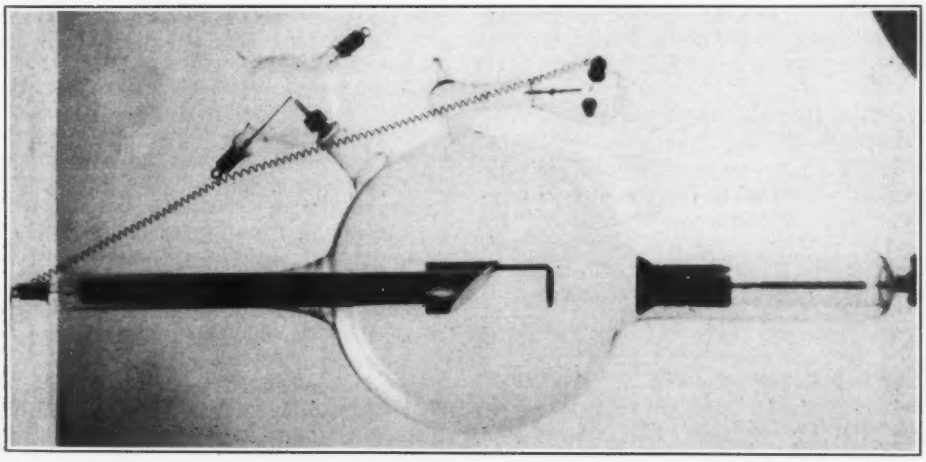

Fig. 6

Hydrogen Tube. Date: 1912 to 1915. Notable features: tungsten target in copper block; focussing ring; double osmotic pressure regulating devices; left hand bulb containing hydrogen at high pressure for increasing pressure in x-ray tube by diffusion through palladium connecting tube, right hand bulb open to air, thus permitting decrease of pressure in x-ray tube by osmotic diffusion of hydrogen out of tube.

the ephemeral vision of an overworked radiologist. In the cold light of scientific development, it has been replaced by the methodical production of tubes in which the delicate grace of harmonious curves has been sacrificed to utilitarian solidity and the precarious results of caprice have given way to stolid dependability.

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EXPERIENCES WITH HYDROPHIL BASES AND SULFONATED PRODUCTS*

By ELMO D. FRENCH, M.D.
Miami, Florida

The ointments ordinarily utilized in dermatologic therapeutics most frequently have as a base excipients of the petrolatum or of the lanolin type.

In a number of ways, petrolatum and lanolin present disadvantages. They hinder rather than promote the activity of substances incorporated in them, for they permit neither adequate dispersion nor solution of active ingredients. They interfere with heat conduction and are impermeable to secretions or exudations. They are objectionable to the patient because difficult to remove from the person or the clothing and because lanolin in particular has a sticky, unpleasant quality.

The usual type of aqueous lotion has certain disadvantages.

Lotions as a rule contain solutions of ionizable substances or suspensions in water of inert powders, or both. Glycerin and ethyl alcohol are often used as solvents and vegetable gums such as tragacanth, karaya and quince are at times added to increase viscosity and adhesiveness.

In lotions of this type, only substances containing easily dissociated ions can be utilized. The surface tension of water is too great to permit penetration or adsorption. Ethyl alcohol incorporated in sufficient concentration lowers surface tension, but is often irritating. On evaporation, the vegetable gums adhere to the skin as an insulating film.

Certain disadvantages pertain to emulsions of the oil-in-water type. They contain at times soaps which have been formed by the union of alkalies with the free fatty acid present in animal or vegetable oils. Such an emulsion may be objectionable because of its alkalinity or because it will not allow the incorporation of strong electrolytes or because of the poor dispersion of the unsaponifiable portion of the oil.

Again, the use of ordinary soap as a detergent is at times undesirable.

Soaps being formed by the union of weak fatty acid radicles with strong inorganic base, as in ordinary sodium, potassium or calcium soaps, or by the union of fatty acid with an organic base, as in triethanolamine soaps, are irritating to the tissues because of their strong alkalinity. They are also ineffectual in acid media and form insoluble lime soap in hard water. If an attempt is made to neutralize the soap solution, as by adding acid, part of the free fatty acid separates from the solution and the detergent properties of the soap are greatly reduced.

Efficiency of these different types of topical applications can be improved therefore, as follows:

By the use of ointment bases which permit of ready dispersion of colloids and of crystalloids and bases capable of absorbing water and not unpleasant to use. By the use of aqueous lotions that lower surface tension, containing solvents that do not irritate, and in which the inert powders are well dispersed, and lotions that do not leave an adherent film after evaporation. By the use of oil-in-water emulsions, which, in addition to the desirable factors improving aqueous lotions, permit the incorporation of stronger electrolytes and are nearly neutral or acid in reaction. Finally topical applications can be improved by the use of detergents that are neutral or acid in reaction and do not readily dissociate to form insoluble curds in alkaline waters.

Unna, in 1912, isolated the water-absorbing ingredients of lanolin and termed them iso- and oxycholesterin. Oxycholesterin was then combined with paraffin. This base absorbed 200 per cent of its weight of water. The high melting point of paraffin did not permit water soluble ingredients to be held in combination, so later petrolatum was substituted for paraffin and this wax sold under German patent rights as "eucerin."

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*Read in Section on Dermatology and Syphilology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

The price of "eucerin" became prohibitive during the World War and domestic manufacturers devised new absorption bases.

Cholesterol added to petrolatum has been recommended as an absorption base. Polycyclic sterols and aliphatic alcohols of high molecular weight are offered under various trade names and are often combined with lanolin, spermacetti or beeswax.

A great variety of formulas result, but from the standpoint of dermatologic therapeutics a few stable absorption bases meet the requirements and only those which I have used without undesirable side effects will be described.

IMPROVING THE BASE

Cetyl alcohol is a white, odorless, waxy powder soluble in alcohol and ether. Its ester, cetyl palmitate, is the major constituent of spermacetti and this was the main source for some time, but it is now prepared synthetically. Cetyl alcohol is absorbed by the skin and retained by the epidermis, rendering it soft and velvety. It mixes with both animal and vegetable oils and fats and when so combined or emulsified it becomes hydrophil and water may be added.

"Tegolan"* is a synthetic wax containing 40 per cent cholesterol. It may be combined with oils, fats or waxes, giving a cholesterol value to the finished product, and may be used instead of lanolin for this purpose. The usual stickiness of lanolin is thus avoided.

Peanut oil, oleum arachis, is one of the most stable of the vegetable expressed oils and does not become rancid readily. An all-purpose base of the oil-in-water type may be formulated as follows:

White wax	10 parts
"Tegolan"	10 parts
Cetyl alcohol	10 parts
Peanut oil	70 parts

This base will absorb many times its weight of water. It is easily removable from the scalp or other hairy parts. Active and inert substances are well dispersed and either salicylic acid may be incorporated up to 50 per cent or sodium hydroxide to 40 per cent.

When 90 per cent of water is added to the base, penetration into the skin of salicylic acid, as shown by Moncorps,[1] is seventy times greater than when a base containing little water, such as lard, is used.

Fungicidal and bactericidal agents are greatly enhanced in power in water-in-oil bases.[2]

Another type of base which is greaseless and to which may be added strong acid is one of the oil-in-water type such as

"Tegacid"*	20 parts
Aqua dist.	80 parts

(A preservative must be added to prevent mold.) "Tegacid" is an acidified glyceryl monosterate. It is a white, waxy substance miscible with water in all proportions.

Zinc oxide and alkalies break this cream.

By adding ½ to 1 per cent phenol and 1 to 3 per cent tartaric acid, I have found this base of value in certain cases of simple pruritus.

IMPROVING THE LOTION AND THE OIL-IN-WATER EMULSION

A remarkable group of organic compounds, possessing surface activity in aqueous media, has been developed and is finding frequent use in the textile, paint and rubber industries, agricultural and other fields. They have been termed "wetting agents." There are said to be over a thousand patents registered for such preparations.

"Aerosol O.T."* 100 per cent is the trade name for the dioctyl ester of sodium sulfosuccinate. This sulfated fatty acid soap has remarkable wetting, penetrating, dispersing and emulsifying properties. It is soluble in oil up to 10 per cent and water to 1.5 per cent. It is stable in acid, neutral and mild alkaline solutions. These properties are useful in the formulation of scalp lotions, as for example:

Salicylic acid	2 parts
Resorcin	2 parts
Diethylene glycol	30 parts
"Aerosol" 1 per cent qs	100 parts

The property termed "wetting power" is based not only upon the reduction of surface tension of a solution, but also reduction of the interfacial tension between solids and liquid. "Aerosol" in the above formula not only does this, thus bringing the dissolved substances in intimate contact with the diseased scalp, but also aids in the dispersion of the active ingredients and emulsifies the seborrheic elements, rendering the scalp easily lavable. Diethylene glycol acts as a solvent and is not irritating as is ethyl alcohol at times.

*"Tegolan" and "Tegacid," manufactured by the Goldschmidt Corp., New York, New York.

*"Aerosol O. T.," manufactured by the American Cyanamid and Chemical Corp., New York, New York.

TOXICOLOGY OF "AEROSOL O.T."*

Extensive feeding experiments carried out on young growing rats at one state college and independent experiments on guinea pigs at another state college demonstrated that "aerosol O.T." is not toxic internally. Locally it has been applied to 200 human wounds by means of gauze dressings without harmful effects in another series of tests.

IMPROVING DETERGENT OR CLEANSING AGENTS

The wetting properties of sulfonated fatty acids decrease, while their detergent properties increase with increase in molecular weight. An organic compound having less wetting power but greater detergent power than "aerosol O.T." is sodium lauryl sulfate.† It is obtained by the sulfonation of lauric acid, a higher fatty acid than that from which "aerosol" is obtained. One per cent sodium lauryl sulfate added to ointments containing tar renders the tar lavable.

The following cleansing formula was suggested for use in acne by P. Cuilleret and M. Gattefossee,[3] who contend that a cleanser of acid pH is to be preferred in acne:

Diethylene glycol	200 parts
13 per cent sodium lauryl sulfate	200 parts
Rose water qs.	1000 parts

This is to be applied with a cotton pledget and rinsed with hot water, once daily. Soap is interdicted.

Diethylene glycol is a solvent, miscible with water and in more than 10 per cent concentration has been found to inhibit the growth of bacteria and fungi.[4] It is non-toxic externally, but quite toxic internally, becoming oxidized into oxalic acid.

I have used the above formula in selected cases of pustular acne for more than two years. It is pleasant to use and quite effectually cleanses. No untoward effects from its use have been noted.

Recently a ten days' test was made on 31 unselected nurses between the ages of 17 years and 20 years, using the following modification of the above formula as a facial cleanser. The directions for its use were the same.

Diethylene glycol	200 parts
13 per cent sodium lauryl sulfate	200 parts
"Aerosol O.T." 1 per cent qs.	1000 parts

The drying effect of this latter formula was considerably greater than the former, which did not contain "aerosol." Fourteen out of the 31 tested manifested, after ten days, excessive dryness. Some in addition had irritative vesicles about the mouth or forehead, but of mild degree. Three of the group having moderately severe acne showed improvement of their acne and desired to continue the use of the formula. Inasmuch as these volunteers were unselected, only a few having any appreciable degree of seborrhea or acne, the experiment was interpreted to indicate the formula's desirable effects under proper conditions.

Sulfonated oils of still higher molecular weight or mixture of such oils are being utilized by the medical profession today as neutral or slightly acid detergents in substitute for soap.

Sulfonated oils are made in general by the action of sulfuric acid on animal or vegetable oils. They have the property of being miscible with water.

"Acidolate," a mixture of sulfonated olive oil, mineral oil, sulphonated rice and tea seed oil is a product of this nature. It is offered by the manufacturer as a skin cleanser. Recently there have appeared upon the market various types of "soapless shampoos." They contain usually sulfonated oils or sulfonated fatty alcohols which have been neutralized with sodium or potassium hydroxide. They are nearly neutral in reaction, but those made of sulfonated oils especially have a greasy feel and do not form a lather. From the patient's standpoint they are not acceptable.

Sulfonated oil products are patented and the process of their manufacture and many of the ingredients of the finished product are a closely guarded trade secret. They are usually of complex structure and have been formulated with an eye to overcoming problems peculiar to the particular industry in which they are utilized. The hydrogen ion concentration of the finished product may be on the strongly acid or alkaline side and organic solvents such as carbon tetrachloride, solvent naptha, benzine, turpentine and trichlorethylene are at times added. Certainly many sulfonated products would prove unfit for use in therapy.

If we are able to define our needs, however, new and effectual agents are now at hand ready to be modified to suit our purpose.

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*Photostatic copies of toxicity tests upon "aerosol O. T.," formerly termed "alphasol O. T.," furnished by the American Cyanamid and Chemical Corporation.

†Sodium lauryl sulfate, manufactured by R. F. Reyson Co., New York, New York.

SUMMARY

Some of the undesirable features to be avoided in ointments, lotions, emulsions and detergents are mentioned.

The incorporation or substitution of certain newer organic substances is suggested, either to correct these faults or as additional therapeutic agents.

A brief description of these new agents and their action, together with several experiences in their use are included.

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DISCUSSION (*Abstract*)

Dr. J. L. Pipkin, San Antonio, Tex.—The improvement of bases is due mainly to the addition of organic compounds which act as efficient emulsifiers. Of the innumerable emulsifiers, cholesterin and lecithin are probably most commonly used. Recently the higher fatty alcohols and their phosphated esters have been added to hydrocarbon bases, making another hydrophilic base available. For example, such alcohols as cetyl and sterol, or a commercially available phosphated mixture of these called "lanette wax," are ideal emulsifiers.

Greater possibilities of improving dermatologic bases are now at hand with the recent adoption of certain organic compounds, which are generally known in industry as wetting agents. The agents of particular interest to us can be roughly classed as sulfonated alcohol and sulfonated esters. Sodium lauryl sulphate ("duponal," M. E. Dry) which is obtained from lauryl alcohol, is a classical wetting agent.

It is noteworthy to make the following observations in regard to these wetting agents.

(1) They are very efficient emulsifiers; therefore, very little of the chemical is required.

(2) Some drying or defatting action on the skin and hair is observed, and if used in high concentration dermal irritation is prone to occur.

(3) The resulting emulsified base is reputed probably to be more penetrating, consequently a lower concentration of the active ingredients should be used.

You notice that I said, "is reputed to be more penetrating." That never has been definitely proven, but various claims have been made.

By judicious use of the cholesterin preparations, the higher fatty alcohols and their derivatives, Dr. French has given us several preparations which should prove of value.

The peanut oil cetyl alcohol cholesterinized emulsions appear to be very useful. We have used a peanut oil emulsion, stabilized with pectin, for some time and found it very satisfactory. The glyceryl mono-stearate oil-in-water emulsion is an extremely smooth and an easily handled base, but it has its limitations, being incompatible with free organic acids and soluble electrolytes.

My experience in using sodium lauryl sulphate as a wetting agent has been mainly with the smooth emulsified petroleum base, as suggested by Duenling. Most of you are familiar with that formula, in which he uses spermaceti, sodium lauryl sulphate and cetyl alcohol as the emulsifying preparation. He uses, roughly:

Mineral oil	15	per cent
Paraffin	10	per cent
Spermaceti	20	per cent
Cetyl alcohol	15	per cent
Water	47.5	per cent
Sodium lauryl sulphate	1	per cent
Stenol	5	per cent
Perfume		
Coloring		

You notice the wetting agent is small in proportion.

The product made by this formula by our local chemist is comparable with the available commercial preparation. We have found no incompatibilities with this base. We find it easy to remove from the scalp, and have encountered no irritation.

We have found it an extremely good base in which to incorporate sulfanilamide or sulfathiazole if we choose to use those things locally.

It has a very definite softening action. If it is put on in thin layers and bound up it will soften the epidermis.

The question of sulfonated oils is still in confusion. There are many sulfonated oils available. Some are suitable to use as skin detergents as a substitute for soap. However, some are irritating and due to the multiplicity of oils used, a specific allergic reaction is encountered. Time alone will tell which sulfonated oil or combination of sulfonated oils will be acceptable for detergents for human skin.

As a general rule, dermatologists cannot intelligently talk to pharmaceutical chemists. They know very little about these matters. We ought to study them and learn some way to improve this situation.

Dr. French (closing).—We cannot increase our skill in the use of topical remedies without the cooperation of an enthusiastic and well trained local pharmacist, who has both pride in his skill in compounding a formula and an interest in the results obtained by its application. This interest he must weigh against the greater profit accruing from the sale of a stock formula, manufactured for mass consumption.

I have been fortunate in having the cooperation of a skilled and enthusiastic pharmacist in Miami.

Products like the sulfonated oils must find their proper niche in our armamentarium almost by a method of trial and error.

Various manufacturers of the latter products show a whole-hearted willingness to cooperate.

THE EFFECT OF THE FEMALE SEX HORMONES ON INFECTION AND INFLAMMATIONS*

By DOUGLAS H. SPRUNT, M.D.
Durham, North Carolina

Clinicians have observed for a number of years that pregnancy modifies the response of women to certain diseases. For example, Kemp[1] reviews the rather extensive literature on the effect of sex hormones and pregnancy on the course of syphilis. He agrees with preceding workers that pregnancy modifies the course of syphilis, but is not able to confirm their conclusion that the same effect may be achieved with estrogenic hormones. Diddle and associates[2] report on an epidemic of scarlet fever on an obstetrical ward and show conclusively that the incidence of scarlet fever among the pregnant women was much less than the incidence among either the attendants or the puerperal women. Rosahn and associates[3] showed that pregnancy increases the resistance of the rabbit to infection with the virus of vaccinia. There are many other reports, but most of them contradict one another. It is beyond the scope of this paper to attempt to evaluate these differences. Suffice it to point out that some of these disagreements are due to failure of the writers to distinguish between effects of pregnancy and those of parturition and lactation, and others are due to failure to distinguish between the localized effect of pregnancy on the sex organs due to changes in morphology and vascularity and the more general effect.

In addition to the changes produced by pregnancy several workers have studied the local effect of certain of the sex hormones. Ziskin and associates[4] found that pregnancy and the estrogenic hormones produce a change in the mucosa of the mouth which makes the gums more resistant to infection. Huberman and Israeloff[5] showed that the gonococcal vaginitis in children could be cured by the estrogenic hormone. Aycock[6] made monkeys more resistant to nasal instillation of the virus of poliomyelitis by changing the character of the nasal mucosa with the estrogenic hormone.

In our experiments we have studied the general effect of the estrogenic hormone and pseudopregnancy on the rabbit. We have avoided the localized effect on the sex organs by limiting our studies to the skin and have not used the skin adjacent to the breasts.

It was considered desirable that these studies be quantitative. Since it is possible to determine with a high degree of precision the amount of the virus of vaccinia needed to produce a lesion in the rabbit's skin, this was chosen as the first factor to be studied.

To determine precisely the amount of virus needed to cause infection, it is first necessary to determine the approximate amount needed. This is done by the inoculation of decimal dilutions of the virus. Then 20 or more inoculations of each of 7 twofold dilutions of the virus are

Table 1

Experiment	No. of Inoculations per Dilutions	50 Per Cent Point 10^{-}	Mean Spread of Ink at Four Hours
Control castrates	24	8.79	cm.²
1. Castrates with estrogens	31	8.41	
Difference		0.38	
Control males	32	9.72	6.47
2. Pseudopregnant	60	9.38	6.01
Difference		0.34	0.46
Control males	46	9.18	8.96
3. Pseudopregnant	33	8.93	6.25
Difference		0.25	2.71
Control males	48	9.36	8.95
4. Pseudopregnant	45	9.18	6.57
Difference		0.18	2.38
Control males	28	6.01	10.53
5. Males with estrogens	28	5.77	8.55
Difference		0.24	1.98
Control males	28	6.54	10.83
6. Males with estrogens	23	6.20	9.04
Difference		0.34	1.79
Control males	28	3.90	——
7. Males with estrogens	28	3.61	——
Difference		0.29	

*Read in Section on Pathology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Department of Pathology, Duke University School of Medicine, Durham, North Carolina.

made. The range covered by these twofold dilutions is so chosen that all of the lower dilutions will give lesions and only a few of the inoculations made from the higher dilutions will be positive. The end point is taken as that dilution from which 50 per cent of the inoculation will give lesions and 50 per cent will not. The results of a number of such experiments are given in the table. Since in these experiments it was observed that the lesions produced by vaccine virus in the treated rabbits were smaller than in the controls it was thought likely that at least one of the factors causing this increased resistance was the ability of these hormones to limit the spread of particulate matter in the skin. Extensive study of this phenomenon in the rabbit's skin shows clearly that both pseudopregnancy and the estrogenic hormone significantly reduce the spread of particulate matter in the skin. The details of these experiments have been published elsewhere.[7]

DISCUSSION

From these experiments it is obvious that the estrogenic hormone and the hormones associated with pseudopregnancy increase the rabbit's resistance to infection with vaccinia. It was also shown that these hormones decrease the spread of particulate matter in the skin. It is thought that the increased resistance of the rabbits with these hormones is due at least in part to the concentration of the infectious agent. The work of Duran-Reynals,[8] although his experiments are the converse of ours, lends support to this hypothesis. In his work he shows that an aqueous extract of the testis will increase not only the spread of particulate matter in the skin, but will also increase the size of lesions produced by a given amount of vaccinia. If, however, this same testicle factor is mixed with a staphylococcus of only moderate virulence, instead of producing a larger lesion as with the vaccinia, no lesion at all is produced. From this work and from ours it is apparent that the spread of vaccinia enhances its ability to attack the rabbit's skin and that its concentration depresses its ability to attack. We are at the present time studying the effect of concentrating other disease incitants and although as yet we have not conclusive evidence we believe that the ability to produce lesions of some, as is indicated by Duran-Reynals' work with the staphylococcus, is enhanced by concentration.

In conclusion, although realizing that considerable more work is needed, we would suggest that pregnancy and certain of the hormones associated with pregnancy aid the host by localizing the disease incitant, while other disease agents may be aided in their growth by this same type of localization.

SUMMARY

Experiments are described which show that the estrogenic hormone and pseudopregnancy increase the rabbit's resistance to infection with vaccinia and also limit the spread of vaccinia in the skin. It is suggested that the increased resistance is the result of the localization of the infectious agent.

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Discussion follows paper of Dr. Rigdon, page 295.

EFFECT OF VITAMINS ON INFECTION AND INFLAMMATION*

By E. WHITE PATTON, M.D.
Nashville, Tennessee

For many years physicians have realized that a satisfactory nutritional status is essential if man is to combat infection with optimal resistance. But only recently have we demonstrated the relationship of vitamins to the maintenance of adequate nutrition. Following this development, many studies have been designed to evaluate the influence of individual vitamins upon resistance to infection. In general, the results have been inconclusive and conflicting. Only a deficiency of vitamin A or vitamin C seems to influence infection in experimental animals, and yet clinically there is very little evidence that a moderate deficiency of these two vitamins materially influences this process. There is no

*Read in Section on Pathology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee.

satisfactory evidence of such an influence when vitamins are administered to subjects who are not deficient.

Before proceeding, it seems advisable to discuss some of the possible explanations of the unsatisfactory results obtained when cause and effect relationships between vitamins and infection have been sought. The most obvious experimental error has been the failure to produce an isolated, single deficiency. This error may express itself in two ways. On the one hand, dietary limitation may be so severe that many vitamins as well as general nutrient factors may be lacking, consequently one sees the effect of a poor general nutritional state rather than that of the particular vitamin. On the other hand, with poor objective measures of the inadequacy of a specific vitamin, actual avitaminosis was often not obtained. Hence the results represent the difference between adequate and super optimal nutrition rather than between inadequate and adequate nutrition. A similar source of confusion in clinical studies has been the tendency to compare the frequency and severity of infection in a selected group exhibiting some deficiency, for example rickets, with a control group, clinically not rachitic. Such differences as exist are explained by the lack of vitamin D specifically. We know now that human deficiency states rarely occur singly, even though there may be only one clinically apparent deficiency; hence many vitamins other than the specific vitamin considered may influence the results. A second mistake has been the failure to recognize the proper cause and effect relationships between vitamins and infectious diseases. The tendency has been to place undue emphasis on the occurrence of lowered body stores of the vitamins during the course of the disease, inferentially attributing the severity of the disease if not its actual incipiency to the avitaminosis. Actually we now feel that these occurrences represent for the most part an increased need for the vitamin due to altered and accelerated body processes. However, such a disparity between the increased demand and inadequate intake, when chronic and progressive, may result in changes unfavorable to the individual's defense mechanisms. A third difficulty has been the traditional unreliability of conclusions obtained from animal experimentation when applied to man. This unreliability is particularly likely to occur when one studies the effect of vitamins on infection and resistance. Apparently the effect of vitamins in this respect is expressed through the mechanisms of intrinsic tissue resistance rather than through mechanisms of acquired resistance. Obviously this is a source of much confusion since different species differ markedly in their intrinsic tissue resistance to infection. And finally an error occurring much too often in the earlier work on this subject has been the lack of adequate controls. The fallacy of attributing to vitamins the differences in morbidity and mortality in two groups of scarlet fever patients studied in different years is obvious when the natural variation in the intensity of the particular disease is considered.

In considering the reasonably well established evidence relative to the effects of vitamins on infection and inflammation, I should like to utilize the broader concept of infection which includes all the complex local reactions comprising inflammation as well as the more general reactions, including the immune response. For the sake of simplicity it seems best to consider the effect of vitamins on (1) susceptibility to experimental and natural bacterial invasion, (2) on tissue reaction and local resistance, and finally (3) on acquired resistance or acquired immune bodies. An attempt will be made to associate the vitamins with these three broad subdivisions of the process of infection and inflammation only when this association seems reasonably well established. No attempt will be made to review the literature or include all evidence suggesting such associations. Virtually all the known vitamins have at some time been suggested as participants in each of these three arbitrary subdivisions of the process. Such clinical evidence as substantiates these associations will be considered separately, since clinically the vitamin effect is frequently a summation of several of these associations.

(1) Susceptibility to experimental and natural bacterial invasion.

Most of the work on the effect of vitamins on infection and inflammation consists of evaluating the influence of their deficiency on susceptibility to bacterial invasion. Of the experimental work, only the studies on vitamin A deficiency are outstanding. In animals the most pronounced changes due to vitamin A deficiency are noted in the specialized columnar epithelium which normally covers the nasal mucosa, trachea, bronchi, and other tissues. Small foci of proliferating squamous epithelium spread out and undermine the columnar epithelium, which in turn degenerates and is desquamated. The foci eventually coalesce and the original columnar secreting epithelium is completely replaced by gland-

less squamous epithelium. In man this process of proliferation and keratinization has been noted also in the skin, particularly about the hair follicles. As a result of these changes several factors may operate to enhance tissue susceptibility to infection. First there is a reduction or loss of mucous membrane secretions. Secondly, epithelial debris, particularly in glands where ducts have been blocked, offers a favorable medium for bacterial growth. And finally it is possible that the replacement epithelium is intrinsically more permeable to invasion than the normal epithelium. Numerous experimental studies in animals have clearly shown that vitamin A deficiency does increase the susceptibility of the animal to infection, certainly locally and possibly generally.

Vitamin C and various fractions of the vitamin B complex have been shown to be essential to the structural and functional integrity of epithelium. Consequently many have felt that vitamin C deficiency and vitamin B complex deficiency might increase susceptibility to infection in a manner similar to that of vitamin A. Recent studies indicate that this may be true experimentally. Topping and Frazer[1] have recently shown that the mouths of monkeys are quite susceptible to invasion by the common oral organisms and saprophytes if the monkeys are rendered deficient in vitamin C or the B complex.

(2) Effect of vitamins on tissue reaction and local resistance.

Of the many experimental studies on the effect of vitamins on tissue reaction and local resistance, only those involving vitamin C deficiency seem well established. Experimentally, in both man and lower animals, a deficiency of vitamin C leads to inadequate production of intercellular cements and poor production of collagen for scar formation. Hence it is important in preserving the functional integrity of all tissues, particularly of the vascular system, and it regulates one of the important phases in the process of healing. As one would expect, there is considerable experimental evidence that a deficiency of vitamin C materially decreases the animal's ability to cope with infection.

Other factors in the maintenance of natural resistance, such as phagocytosis and complement titer, have shown no consistent variations as a result of vitamin inadequacies. Recent work indicates that complement titer is definitely lowered in scorbutic animals, but in view of previous controversial results judgment on this must await further studies.

(3) Effect of vitamins upon acquired resistance and acquired immune bodies.

Definite evidence of vitamin influence on the production or activity of acquired resistance is meager. Some experiments suggest that vitamin C may modify antibody formation, and others indicate a detoxification of certain toxins *in vitro*. There is no clear, experimental evidence that any of the vitamins modify the acquired resistance elicited by infection.

When one turns from the experimental to the clinical reports of the effect of avitaminosis on infection and inflammation the majority of the more convincing studies deal with the influence of vitamin A and vitamin C. This seems quite logical since the majority of the reasonable experimental work deals with the influence of these same vitamins.

Block[2] has reported that children suffering from xerophthalmia are extremely liable to severe infections, and that even after the deficiency is corrected, this increased susceptibility to infections continues for years. The majority of those who have investigated the effect of severe deficiency of vitamin A agree with the opinion of Block. The results of those who have studied the effect of milder deficiencies of vitamin A have been quite variable. Clausen[3] has analyzed the blood of a group of children for carotene and vitamin A. The average value for blood carotene was lower in the group with histories of frequent respiratory infections, but he feels that the increased susceptibility to infection attributable to this factor is relatively slight. Other studies on mildly deficient subjects indicate that vitamin A supplements probably do not decrease the frequency of infections, but may decrease the duration and severity of the infections. Administering additional vitamin A to subjects in whom no deficiency exists does not seem to influence the incidence or course of an infection in such individuals. Hence it seems likely that severe vitamin A deficiency predisposes to infection; that mild vitamin A deficiency contributes to the duration and severity of an infection; and that the effect of excessive vitamin A intake on infections is negligible. It should be pointed out, however, that probably

no vitamin A deficiency existed in many of the experimental subjects who were supposedly mildly deficient, and that with improved objective methods for determining the presence of a deficiency, future results may differ from those of the past.

The preponderance of the clinical studies on the effect of vitamin C on infection has dealt with the occurrence of avitaminosis C in the course of infectious diseases. There are many conflicting reports as to the results obtained when vitamin C is administered during the course of such diseases. At present the most favorable reports result from the administration of vitamin C in pneumonia, pertussis, and rheumatic fever. There are numerous clinical studies substantiating the experimental demonstration that vitamin C deficiency delays scar formation in the process of local healing. However, a recent study in experimental human vitamin C deficiency[4] suggests that this occurs much later in the course of a deficiency than was previously presumed.

In summary it is quite evident that the demonstrable effects of vitamins on infection and inflammation are few. Future studies may be more revealing. Little is known of the functional interrelationships of the vitamins, and of their active and passive relationship to the glands of internal secretion. Improved objective methods of determining the presence and degree of a vitamin deficiency will be of considerable aid in evaluating the action of vitamins. But at the present, as much as one might like to make a definite contribution to this symposium, the available evidence on this subject justifies only this cautious conclusion. A severe deficiency of vitamin A or of vitamin C apparently decreases the body's ability to cope with infection, but the influence of moderate individual vitamin deficiencies is extremely uncertain.

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Discussion follows paper of Dr. Rigdon, page 295.

RELATION OF CAPILLARY PERMEABILITY TO INFLAMMATION*

By R. H. Rigdon, M.D.
Memphis, Tennessee

The mechanisms of the occurrence of the cardinal signs and symptoms of inflammation have been studied extensively since the time of Cohnheim. Some of the phenomena, however, are not well understood even today. One important problem is that of increased capillary permeability.

Variations in permeability of the small blood vessels are demonstrated by intravenous injections of different types of materials. Those most frequently used are trypan blue, graphite particles, and suspensions of india ink. The localization and the concentration of these in a specific area are considered indicative of an increase in the permeability of the small blood vessels. It is stated by Menkin[1] that "Trypan blue and other dyes introduced into the circulating blood promptly accumulate in an inflamed area." Burrows[2] says "The walls of the blood capillaries of an inflamed region are pervious to colloids, and indeed to substances whose particles are of a larger size. These substances * * * will leave the blood vessels and, entering the inflamed tissues, will be retained by them." It is obvious from Menkin's and Burrows' studies that wherever there is inflammation there is an increase in the permeability of the small blood vessels.

It has been shown recently by Rigdon[3] that trypan blue following an intravenous injection in the rabbit may fail to localize and to concentrate in areas of inflammation produced by the local application of xylol, although there are edema and hyperemia, and polymorphonuclear leukocytes are present in the extravascular tissues.

All investigators do not agree upon the method by which colloids reach the extravascular tissues. Florey[4] has shown that colloids and crystalloids pass directly through the cytoplasm, but not through the nuclei of the endothelial cells of the capillaries. Krogh[5] once considered that an increase in permeability is accompanied by the opening of fissures between the endothelial cells of the capillaries. He thought that any

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*From the Department of Pathology, University of Tennessee.

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stretching of the capillary wall would increase capillary permeability. Landis[6] has shown, however, that there is no difference between the permeability of wide and narrow capillaries.

It appears to be the opinion of most investigators that some substance or substances are liberated from injured tissue. These act upon the blood vessels to produce both the changes in the diameter of the vessels and the increase in permeability of the endothelium. Ebbecke,[7] in 1923, postulated that such a substance is formed by irritated epithelium which diffuses to the capillaries and smaller arterioles. Lewis[8] attributes the reaction to the liberation of a chemical H substance by the injured tissue. Krogh[5] postulates the presence of two substances liberated from injured cells: a diffusible factor closely related to histamine, if not histamine itself; and an H colloid substance which is probably less diffusible. Menkin[1] recently has isolated a crystalline nitrogenous substance from inflammatory exudates which induces a prompt increase in the permeability of normal capillaries. This he calls leukotaxine. According to Menkin,[1]

"The factor is evidently not a protein, yet it contains amino and carboxyl groups. It gives a positive test for the presence of an indole nucleus in its structure (Adamkiewicz test). The active material in exudate is dialyzable; and it is precipitated by concentrated ammonium sulfate. The present evidence suggests that it is an intermediary breakdown product of protein metabolism, possibly belonging to the group of relatively simple polypeptides. The active factor manifests no property in common with histamine or presumably with the hypothetical H substance assumed to be closely related to histamine. Observations do not substantiate Lewis' hypothesis of histamine or of its closely related H substance as the primary cause of increased capillary permeability in inflammation."

According to Menkin,[1] leukotaxine induces a rapid migration of polymorphonuclear leukocytes through the wall of small vessels into the cutaneous tissue.

Rigdon[9] has shown that a saline extract of skin, muscle or testicle from normal rabbits when injected intradermally produces an increase in capillary permeability as shown by the localization and the concentration of trypan blue in the skin following an intravenous injection of the dye. Polymorphonuclear leukocytes also localize in the extravascular tissue in the areas where these saline extracts are injected. Bier and Planet's[10] results with extracts of normal rabbits' tissues are the same as those of Rigdon.

There apparently can be no question that the crystalline substance isolated from an inflammatory exudate produces an increase in capillary permeability and the localization of polymorphonuclear leukocytes in an area where it is injected.[1] However, in view of the fact that trypan blue localizes and concentrates in the skin following the intradermal injection of many different substances, it is suggested that this phenomenon of localization and concentration of dye is not primarily the result of the presence of a single crystalline substance.

The interval during which trypan blue localizes and concentrates in areas of inflammation is variable. This dye localizes and concentrates for approximately three hours in an area of inflammation produced by the local application of xylol in the rabbit's skin. The greatest quantity of dye localizes in the area where xylol is applied for the shortest interval before the dye is given. There is a progressive diminution in the quantity of dye present in the xylol treated areas when the interval between the application of the irritant and the injection of the dye is increased.

When staphylococci are given intradermally, the greatest quantity of trypan blue localizes in the skin where the bacteria are injected from 45 to 90 minutes prior to the intravenous injection of the dye.[11] Smaller amounts of trypan blue localize and concentrate at the periphery of abscesses produced by staphylococci. The exact time for the localization and concentration of dye in areas of inflammation produced by bacteria is difficult to determine. The data from other experiments suggest that the dye localizes and concentrates at the periphery of bacterial abscesses as long as the infection is progressing.

The interval during which trypan blue localizes and concentrates in the skin of rabbits made sensitive to horse serum is more definite. The duration of this increase in permeability is longer in the sensitive animal than it is in the normal.[12]

Intervals during which intravenously injected substances localize and concentrate in areas of inflammation have been observed by others.[13] [14] In Fox's[14] experiments,

"Inflammatory lesions of various ages were created in rabbit skin with three types of irritants, and large doses of test materials (trypan blue, hemolytic and agglutinating sera) were injected intravenously. It was found that the youngest lesions localized the dye more rapidly, and in greater amounts than the older lesions. Further, the power to localize blood-borne materials was found to persist for a longer time in lesions produced with the stronger irritants. This was correlated with the persistence of a granulation type of reaction about areas of local breakdown of tissue. Where such breakdown did not occur, the property of localization was lost after 24 hours, apparently because of vascular interference."

In my experiments, occluded capillaries are present especially in the areas where both staphylococci and staphylococcus toxin are injected. However, thrombosed vessels are essentially nil in those areas of inflammation produced by the local application of xylol.[3] Furthermore, a second application of xylol 24 hours after the first permits the localization and the concentration of trypan blue in the inflamed tissue. It is considered unlikely on the basis of the histologic studies and the presence of dye in areas where xylol is applied a second time that the failure of the trypan blue to localize and to concentrate in old areas of inflammation produced by xylol is the result of vascular occlusions.

It is suggested that trypan blue localizes and concentrates in areas of inflammation as the result of a temporary change which occurs in the epithelial cells, the connective tissue cells, and the endothelial cells of the capillaries. This change in the permeability of these cells results from the effect of xylol on the epithelial cells. The normal metabolism of the epithelial cells is disturbed as shown by the presence of pyknosis, karyorrhexis, and necrosis. The results of the effects of this abnormal intercellular fluid on the capillary endothelium is, no doubt, a compensatory mechanism permitting the passage of water and crystalloids at a more rapid rate than normal and also readily allowing the passage through the vessel wall of the cells, colloids and plasma proteins. It must be remembered that the time and the rate that water and crystalloids pass the capillary wall in an area of inflammation may be different from the time and the rate in which trypan blue passes the same capillary wall. In considering this problem, Landis[15] says:

"The migration of these diffusible solutes to which the capillary wall is more or less permeable need not follow the current of water during either filtration or absorption. From present evidence, the passage of these dyes is largely due to diffusion and under ordinary conditions is relatively independent of capillary pressure. Yet, marked elevation of capillary pressure increases the passage of dyes everywhere along the capillary so that under appropriate conditions the filtration of dye-stained fluid can be superimposed upon pure diffusion of dye and may even obliterate evidence of local differences in endothelial permeability."

The capillary endothelial cells are not the only cells to show a disturbed function in the presence of an inflammatory reaction. The blue color of the desquamating epithelial cells in the rabbit following the local application of xylol and the intravenous injection of trypan blue suggest that the dye has been either absorbed or adsorbed by the injured cells. The presence of a large number of vaccinial lesions in the skin of the rabbit where xylol is applied and the virus is given intravenously also suggest that the permeability of the epithelial cells in areas of inflammation is increased. It must be remembered, however, that the increased number of vaccinial lesions in an area of inflammation may result only from the increased amount of virus in the intercellular fluid.

Arey,[16] in 1936, reviewed the changes that occur in the extravascular cells in areas of inflammation and sites the following observations:

"Schmidtmann and Matthes (a) have shown that there is an early increase in the permeability of the surface of the cells of inflamed connective tissue. It is possible that this results in the loss of potassium from the cytoplasm (b) which would then upset the iso-ionic balance of the sodium-potassium calcium content of the fluid, and especially the ratio of calcium to potassium (c). In any event, when cells are injured or inflammation is set up the potassium increases (d, e) and can reach high values (f)."

In addition to the disturbance of the balance of certain salts in areas of inflammation the tissue cells liberate enzymes which lead to an elevation of the local metabolism.[16]

In view of our present knowledge of the effect of environment on tissue cells and the experimental observations on the localization and concentration of trypan blue in areas of inflammation, it appears likely that all the cells in an area of tissue are affected either directly or indirectly by a chemical agent such as xylol.

The time during which trypan blue passes at an increased rate through the wall of the capillaries is brief. The interval appears to be less than that during which there is an increase in the rate of flow of water through the same capillary wall. This is suggested by the variation in the quantity of trypan blue that localizes and concentrates in an area of inflammation produced in the skin of the rabbit by the local application of xylol when the dye is given intravenously at varying intervals following the application of the irritant. Oswald[17] has said that the different proteins leave the vessels in areas of inflammation as follows: albumin, euglobulin, pseudoglobulin and then fibrinogen.

Capillary permeability as studied by the intravenous injection of trypan blue is apparently an illustration of the phenomenon of biological staining, the explanation of which is still theo-

retical.[18] The principle of selective adsorption of dye is well known. Conn[18] has said in this connection:

"Certain ions may be adsorbed by certain substances much more readily than by others * * * the rate of adsorption of any ion is strongly influenced by the presence of other ions in the solution, and any especially profound influence is exerted by the reaction of the solution, in other words by the concentration of free hydrogen or hydroxyl ions in the field; the influence of the latter upon the adsorption of basic ions being exactly the opposite from its effect upon the adsorption of acid ions. Such principles as these * * * afford a reasonable explanation of such phenomena as the differential staining of different cellular elements, action of mordants, variations in rate of staining with changes in the salt content of the staining solutions, and influence of H-ion concentration upon the color assumed by tissue when exposed to the action of both acid and basic dye."

SUMMARY

The observations here suggest that the process in inflammation referred to as increased capillary permeability represents a phenomenon well recognized in vital staining. The staining results from a metabolic disturbance in the epithelial cells, connective tissue cells, and endothelial cells of the small blood vessels. Edema, and hyperemia, may accompany this disturbance in the cells. These two processes, however, are not a prerequisite for the localization and the concentration of trypan blue in areas of inflammation in the skin of the rabbit. The dye may localize and concentrate in tissue when there are no polymorphonuclear leukocytes and fail to localize and to concentrate when the subepithelial tissues are diffusely infiltrated with leukocytes. It may be said at this time that at least two factors influence the interval during which trypan blue localizes and concentrates in areas of inflammation in the skin of the rabbit following an intravenous injection of trypan blue. These are, first, the irritant; and second, the state of sensitivity of the cells as shown in the studies with rabbits sensitive to horse serum.

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DISCUSSION (*Abstract*)

Papers of Dr. Sprunt, Dr. Patton and Dr. Rigdon.

Dr. Melvin H. Knisely, Memphis, Tenn.—On the first paper, I am deeply impressed by the use of mathematics in biological problems.

Some time ago, a dean in a medical school with which I am familiar prevented one of the medical students from taking some advanced mathematics course on the ground that it was useless in medicine. If any of you happen to be deans now, or if you become deans later, I strongly suggest that any student who has nerve enough to study mathematics be thoroughly encouraged. Work of this kind which shows the conditions under which a virulent organism can be retarded and a non-virulent organism accelerated cannot come without mathematics or a mathematically trained mind.

As Dr. Patton pointed out, the problem cannot be analyzed because of failure to isolate single individual factors and examine them all. That again is essentially the thing that mathematics does when you give it a chance.

In order to understand what the vitamin does in protecting the animal, it will be necessary to know the exact mechanisms which can fail. Have we a failure of dry, keratinized epithelial tissues to prevent the penetration of bacteria? Have we a failure of the lymphatic system to filter them out and catch them in lymph nodes? Have we failure of the phagocytic system in the blood stream and failure of the leukocytes? When we know the exact mechanisms with which we are working, we shall be in position to examine in complete detail the mechanisms that fail. Dr. Patton pointed that out very thoroughly.

Dr. Rigdon has shown a method here which permits us to preserve in histologic sections evidence of transitory phenomena which happened when we applied material to the skin to alter permeability. Not only is the

endothelium damaged, but the epithelium and connective tissues, and each of these should be examined separately and combined.

Many different kinds of things can damage endothelium. The facts that you can have a change in permeability and a change in the stickiness of the lining of these vessels, two different phenomena, one one time and another at a different time, are important.

Dr. Wiley D. Forbus, Durham, N. C.—It is an extremely difficult thing to transplant observations such as you have heard discussed by the three speakers, in the experimental animal, to the human being.

It is very important that one shall differentiate with great care between infection and inflammation if one is going to study in any one of the three fields which you heard about.

Inflammation, according to my ideas, is distinctly a localized phenomenon. I do not mean for a moment that there are not generalized and generally related inflammations, but inflammation is essentially a localized process. It is obvious that one cannot talk about a localized process in terms which apply to generalized processes. Let me illustrate. Infection, in contrast to inflammation, as I see it, is something which is general. If an organism is introduced into the blood stream and remains in the blood stream and grows in the blood stream, as it does, we all know it is perfectly possible that no local inflammation shall arise at all, and yet the individual, of course, will die. That is a general thing, as opposed to a thing, for instance, like an abscess, which is distinctly a localized phenomenon.

Now you cannot talk about the general process in terms of the local process, so as I listened here, I felt that it was necessary for one to define his field of thought, and I tried to do that for myself. In these three papers we have had data presented which can be interpreted only in the light of three very broad factors.

The first is we must be concerned with the broad character of the host. Secondly, we must be concerned with the general nature of the agent which is used. Thirdly, we must be concerned with the concentrates of the infectious agent in the environment.

Now, to be a little bit more specific, I should say we shall have to concern ourselves with those factors which influence the invasion of the tissues by the organism, and we shall have to concern ourselves with the things which take place, with the initial things which take place once the organism is in, and then we shall have to concern ourselves with the reactions that follow once the organism is introduced into the tissues.

Now capillary permeability is a thing which I should like to think of principally as the effect of an initial injury, and I think Dr. Rigdon has placed a great deal of emphasis upon that thing. I do not think for a moment, and Dr. Knisely has already expressed this feeling, that there is any one thing which we can say is responsible for an increase in capillary permeability. There must be hundreds of things that can produce that effect.

If you think for a moment of the introduction of bacteria or a gas, let us say, into the lung by way of air passages, I think you will call to mind at once a series of events which illustrates well what I mean by the capillary permeability's being dependent upon the initial injury. Virulent bacteria, when introduced into the lung by the air passages, will produce, first of all, an extraordinary edema of the lung, and that is all that one may be able to see.

Now that fluid obviously has come from the blood vessels, if one is to believe what he knows about the constitution of those fluids, so there is the initial injury with increased permeability at once.

It is also possible that once bacteria are introduced into the lung tissue, substances may develop there which will also influence the permeability of that same blood vessel, and unquestionably that happens. That is the thing, of course, which Menck refers to and has described accurately.

It is very difficult to discuss this thing in any kind of logical fashion, as you can well see, because there are many different phases of the problem. Permeability is a thing which is concerned with the initial effects of injury primarily, and we ought not to think about it in inflammation as something that influences tremendously the inflammatory process once it is established.

I do not know just exactly how much what Dr. Sprunt has found out means toward understanding the processes of inflammation. I think probably it means a great deal from the point of view of understanding the invasion of a body by harmful agents. At the present time, though, it is very difficult for me to see exactly how it can be applied specifically to the inflammatory processes. I do not think he has intended that it should be.

I know a little bit about the vitamins, not a great deal. That little bit is gained in the same way that you have gained your knowledge, most of you, about them. But I have done a little bit more than that. I worked with one of the vitamins, the B_6, two of the B factors, for about eighteen months in an attempt to learn something about its influence upon the cells of the body, particularly the central nervous system. Frankly, I think I learned absolutely nothing about it, and the methods which we used were acceptable methods. The materials which we used were chemically pure substances. So I think we had a fair chance, in a limited way, to learn something about them.

If methods which utilize highly purified chemical vitamins cannot produce good information or sound information, I wonder if we can depend at all upon any of the more general bits of information or pseudo-information that come to us from clinical observations or from observations which are in general of the same character as clinical observations.

So, Dr. Patton, I agree that the situation there is an extremely chaotic one, and surely we must be exceedingly cautious in saying anything at all until better methods have been invented for the studying of the problems which have been discussed.

I am sorry that what I have had to say has had to be haphazard, but, as I promised you, it had to be just a few observations.

Dr. Sprunt (closing).—We have been interested for some time in the relationship of infection to inflammation. It was first thought that these two might be

completely separate; for example, that the incidence of a disease in the pregnant woman might be decreased, but that when the disease actually occurred in a pregnant woman the course might be more severe. In experiments and also in chemical reports we have found this not to be true. When the incidence of a disease is decreased, then the reaction of the host to the disease is decreased. Therefore, we do not believe that infection can be considered separately from inflammation.

EXPERIENCES WITH THE INJECTION TREATMENT OF HERNIA*

By AMOS R. KOONTZ, A.M., M.D., F.A.C.S.
Baltimore, Maryland

I wish to state at the outset that I am neither a protagonist nor an antagonist of this method. I undertook this work for the sole purpose of learning what value, if any, it held.

For many years I have given an elective course on hernia in the Johns Hopkins Medical School, and each year in the course, until the fall of 1935, I have mentioned the injection treatment only to condemn it. The reasons I have always given students for not using the injection treatment have been as follows:

"(1) The injection method does not cure the hernia. (2) Important structures may be injured by the injection. (3) The scar tissue caused by the injection makes operation more difficult when the patient does finally come to it."

However, by the fall of 1935, so many favorable reports dealing with the injection method had appeared in the literature that it seemed to me that I could no longer go on condemning it without having some first hand information upon it. I discussed the matter with Dr. Harvey Stone, and he agreed with me that the method ought to be tried. I then approached Dr. Dean Lewis, at that time Professor of Surgery in the Johns Hopkins Medical School, and asked for permission to try the injection treatment on some of the patients in the Surgical Out-Patient Department. With characteristic crispness, Dr. Lewis replied: "No, you can't do it here." He then asked me: "What is the weakest tissue in the body?" I replied that I considered either adipose tissue or areolar tissue the weakest tissue in the body. His answer was: "No, it is scar tissue."

I was forced to take issue with Dr. Lewis on this point, as everyone knows that scar tissue varies greatly in its character, depending upon its location, and the variable factors concerned in its production. Scar tissue may be a very weak and flimsy material with no strength whatsoever. On the other hand, all of us have seen scar tissue that was enormously strong, and had almost the consistency of cartilage.

Being turned down by Dr. Lewis, I then went across the street to see Dr. Alfred Ullman, Chief of the Surgical Service of the Sinai Hospital, and put the same proposition to him. Dr. Ullman felt, as Dr. Stone and I did, that the method ought to be tried, and very graciously gave me permission to start a hernia clinic in the Out-Patient Department of the Sinai Hospital, which has now been a going concern since January, 1936.

In the fall of 1939, I spoke to Dr. Warfield M. Firor, now Acting Professor of Surgery in the Johns Hopkins Medical School, about starting a hernia clinic in the Out-Patient Department of the Johns Hopkins Hospital similar to the one I had at the Sinai Hospital. Dr. Firor thought the idea a good one, and accordingly the clinic at the Hopkins has been running since February, 1940. This clinic is not a duplication of the one at the Sinai Hospital, as different methods are used in the two clinics.

I shall make no attempt in this paper to discuss the history of the injection treatment, the technic employed, or the relative merits of the various solutions that have been used. These matters have already been discussed at length by writers who have had far more experience with the method than I have.

In an effort to determine the relative merits of the various solutions that have been used for injection, I have used a considerable number of solutions, as follows: "galtanol," "neogaltanol," "proliferol A," "proliferol B," "proliferol T-Special," phenol-alcohol-oil of thuja solution, sylnasol, Mayer's solution, and phenol and glycerine solutions. I am not in a position at present to discuss the relative merits of these various solutions. Several of them have not been in use long enough to compare them with those used early in the series.

The number of cases in this series is small, totaling only 179. I hesitate to report this small series, and am impelled to do so only because I am constantly asked what my results with the injection treatment are, and because I believe reliable workers in any new field should let the

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*From the Surgical Clinics of the Sinai Hospital and the Johns Hopkins Hospital, Baltimore, Maryland.

profession at large know what their results are, so that a proper evaluation of the new method may be made. If we waited until absolutely definite conclusions could be drawn with regard to the injection treatment of hernia, no reports would be made on the method for many years to come.

All but nine of the hernias injected in this series have been inguinal hernias. The series includes all varieties of inguinal hernias: direct and indirect, scrotal and non-scrotal, and recurrent. I have not considered femoral hernias as particularly suitable for the injection method. However, I may try the method on a limited number of cases at some later date. Umbilical and postoperative ventral hernias are not suitable for injection unless they are very small. If, however, they present a fascial defect only 1 or 2 cm. in diameter, the defect can readily be closed by the injection method.

Table 1 shows the results obtained. I have made no attempt to show percentages of cures. The follow-ups have not been good enough, nor the length of time long enough, to make such figures at all worth-while. The average number of injections and the average number of months that each patient was injected are rather high because in some of the older cases the hernias recurred and had to be reinjected. In some instances they recurred twice and were reinjected twice. Also, some cases were given strengthening injections as a precautionary measure months after the regular course of injections was stopped. The total number of injections and the total number of months treated (including the injection of recurrences) are included in each case. The number of short-period cures is rather impressive, while the number of long-time cures is not. This, of course, is partly due to the fact that the series is not an old one. The number of failures has not been large.

Complications.—There have been a fair number of cases in which a slight swelling of the cord followed injection, but in all cases this has subsided in a few days. There have been six cases in which the complication was more severe. In one case there was an epididymitis which subsided without any treatment except the wearing of a suspensory. In one case a small hydrocele developed, which completely disappeared in a few weeks without treatment of any sort. In another case a large hydrocele developed, which persisted. This man had a large scrotal hernia, and the injection treatment was begun on the patient's insistance, and after he had been strongly advised to have an operation instead. After having 38 injections the ring had been materially decreased in size, but the hernia was still not cured, and the hydrocele had developed. The patient then consented to operation, and at operation it was found that he had a sliding hernia. The bottle operation for hydrocele was done, the hernia was repaired with ox fascia, and the patient has remained well for the eighteen months since his operation. Sliding hernias have been considered contraindications for the injection treatment, but it is well known that it is not always possible to make a diagnosis of sliding hernia before operation. In this case, there was no difficulty in keeping the hernia reduced, apparently completely, although obviously not completely. This case shows, however, that if

Table 1

Types	No. of Cases	Av. No. of Injections	Av. No. of Months Injected	No. Cures Less than 6 Mos.	No. Cures More than 6 Mos.	No. Cures More than 1 Year	No. Cures More than 2 Years	Failures	Incompleted or Still Under Treatment	Complications
Indirect inguinal (non-scrotal)	117	21	10	31	18	10	6	3	49	Epididymitis 1 Deep abscess 1 Hydrocele 1
Indirect inguinal (scrotal)	20	31	14	5		2	1	4	8	Hydrocele 1
Direct	15	26	13	1	1	1		1	11	
Recurrent	18	32	23	3	2	3	2	4	4	
Umbilical	4	6	2	2			1		1	Abscess 1 Sinus 1
Ventral (postoperative)	5	6	7	2	1				2	

care is used in making the injections, placing them just under the aponeurosis of the external oblique and not too deeply, a sliding hernia may be injected without serious complication, but necessarily without cure of the hernia.

The most serious complication encountered was the formation of a deep abscess, following an excoriation of the skin due to the pressure of a rather severe truss. A gangrenous area of skin, 1.5 cm. in diameter, developed, and when this was removed the necrotic core was found to go down through the subcutaneous tissue to the aponeurosis of the external oblique. Some of the aponeurosis of the external oblique sloughed away, and the lesion required three months to heal. A lighter truss has been fitted on this patient and the injection treatment resumed.

In one umbilical hernia an abscess formed, which had to be incised, and in another one a small sinus developed, which healed promptly under proper treatment.

In a few instances I have felt sure that the injections have gone into the peritoneal cavity. In these cases there has been generalized abdominal pain, and in some cases narcotics have been administered. In all cases the pain has subsided within a couple of hours, and there have been no untoward results.

I have operated upon several of the failures. While at operation a large quantity of scar tissue was found, the operation was not so difficult as the ordinary operation for recurrent hernia, as there was no distortion of the anatomy which is often found at operation for recurrent hernia.

DISCUSSION

It goes without saying that no hernia should be injected unless it can be kept constantly reduced with a suitable truss. At first I used the semi-rigid variety of truss, but during the last ten months I have been using elastic trusses. I believe that a rigid truss is apt to exert too much pressure and cause too much atrophy of the newly proliferated tissue. Elastic trusses are found capable of keeping hernias reduced, while not causing the marked atrophy that the rigid type causes. Some of the larger hernias are difficult to keep reduced, and in these cases any type of truss that will keep the hernia reduced should be used until the rings are so narrow that a lighter truss will prove efficacious. Trusses should be worn night and day during the first few weeks, after which they may be discarded at night. Naturally, the elastic type truss is much more comfortable to wear in bed than the semi-rigid variety. A great deal depends upon the cooperation of the patient. The truss should not be taken off until after the patient is lying down in bed, and should be put on before he gets out of bed, while he is still lying down. It should be put on if he gets up at night to go to the bathroom. The truss should be worn neither too tight nor too loose nor too high nor too low. The pad should rest just above the pubic bone, and the truss should encircle the body midway between the great trochanter and the crest of the ilium.

As with any new method, naturally, there is still much to learn about the injection treatment of hernia. It has been recommended by some writers that some of the solutions used be injected two or three times a week, while others are injected only once a week. I do not believe that the optimum time that should be allowed to lapse between injections has yet been worked out. Will injections given too closely together destroy new fibroblasts that have been caused to proliferate by previous injection? Will ground be lost by spacing the injections too far apart? So far as I know, sufficient experimental work has not yet been done to furnish the answers to these questions.

In this series patients from all age groups have been injected. Apparently the younger the patient the better the result. The number of children injected has been small, but the results have been uniformly good.

A group of patients in which the injection treatment seems to be especially indicated is the group of old patients with troublesome hernias, in which operation would be too hazardous. I will cite an outstanding example of this group.

This patient, 93 years old, had a scrotal hernia on the right side the size of a grapefruit and a nonscrotal hernia on the left side the size of a tangerine. There had been threatened strangulation several times on the right side, and the patient's son, who was a physician, had referred the patient to Dr. Harvey Stone for operation, and Dr. Stone had had him admitted to the Union Memorial Hospital for that purpose. However, rather than risk operation on a patient of that age unless absolutely necessary, Dr. Stone asked me if I would see the patient and try the injection method on him if I thought it feasible. I was able to keep both hernias reduced with a light truss, and to effect a cure on both sides. The patient died a year later from a stroke, and his son told me that the large hernia on the right side had remained cured until two months before death, when a small recurrence appeared. That on the left side was still cured at the time of death.

This patient was rather uncooperative and could not be made to wear his truss continuously even while the injections were being given. After the injections were over he did not wear a truss at all. Had he worn a

truss, I do not believe that the recurrence on the right side would have ensued.

Another type of hernia that is very favorable for the injection treatment is the recurrent inguinal hernia, in which the defect through which the recurrence appears is small. I have one such patient who was operated upon three times on each side, and each time by an exceptionally competent surgeon. He came to me after the third recurrence, and the recurrence on each side was through a defect only about 1 cm. in diameter. Both of these were injected, and the patient has now been well for three years. Naturally, he is delighted with the result. I have another similar case, injected for hernias twice recurrent on each side, but this case has now been well for only a few months.

There is another type of patient in which I think the injection treatment is especially applicable. I refer to patients of the industrial class who, because of enlarged rings with slight impulses, are denied employment. I have a few patients of this class in whom I have been able to close the rings completely, who are free from impulses, and who have been accepted for employment in arduous tasks.

Patients who receive the injection treatment almost invariably say that they feel much better after they have had a few injections. The uncomfortable dragging down symptoms disappear.

CONCLUSIONS

(1) I believe that the injection method will have a permanent place in the treatment of hernia. Just how wide the scope of this place will be, it will take years to determine. I further believe that the majority of the reports so far published have been too optimistic, and that the number of recurrences in ensuing years will reduce the high percentage of cures in the early reports.

(2) The chances are that the field for the injection treatment will be widened as methods and proliferating solutions improve.

(3) At the present time the injection treatment seems indicated in the following groups of patients:

(a) In old people with difficult hernias that cannot be satisfactorily retained by a truss. Many of these cases can be cured and kept cured if they continue to wear a light truss, while recurrences ensue in a great many of them if the truss is discarded.

(b) In those patients who will not, on account of fear or other reasons, consent to operation.

(c) In those patients who do not feel that they can afford to take time off for operation, either for financial or business reasons.

(d) In patients in the industrial class who have potential, but not actual hernias, and who are refused employment because of this.

(4) The most favorable cases for injection from the point of view of cure are fairly early indirect inguinal hernias, very small umbilical and postoperative ventral hernias, and small recurrent inguinal hernias.

DISCUSSION (*Abstract*)

Dr. Pat R. Imes, Louisville, Ky.—I, too, began the injection method of treating hernia in 1935 by establishing a hernia clinic in the Louisville City Hospital, and later employed it in practice privately. I continued it until 1938, since which time I have practically abandoned the method.

My cases numbered 78, all of which were indirect inguinal in type. I was rather hopeful for the first year because the immediate results were good; however, as more time elapsed and the trusses were discarded, recurrences were the rule. Today I cannot find a single case that is cured in which the truss has been discontinued, and one would expect a better record than that only by the wearing of a truss for a similar period of time. Three solutions were employed: "sylnasol," "proliferol," and the oil of thuja mixture, and no difference could be detected in the ultimate results following their respective use.

In addition to the qualities of fibrous tissue mentioned by Dr. Koontz, I would add that of absorption. It was a common experience practically to occlude the external inguinal ring with a few injections, and within six months little or no evidence of the injection could be detected on examination.

My experience in regard to the complications from the injection is in accord. There was no complication of consequence following well over a thousand injections.

My patients were enthusiastic and stated almost invariably that they felt relieved of any previous discomfort. I agree that hernias can be more easily retained by a truss by supplementing with a few injections, but I doubt that the truss should ever be discarded. I also agree that men who have been refused employment because of a so-called potential hernia can have the external ring tightened up at least long enough to pass the examination.

I shall resume more general use of the method when some substance is found which, when injected, will produce more prolonged relief.

Dr. J. M. T. Finney, Jr., Baltimore, Md.—I have had no experience with injection treatment, and I am afraid I am one of the rather hide-bound surgeons who has felt it was definitely a non-surgical procedure, and as such was not worthy of notice.

That is a dangerous attitude to assume in regard to anything, because we not infrequently have to change our tactics completely at a later date. New things are apt to be non-appealing at first. Certainly that was the case at the start of the injection of varicose veins, and yet I believe almost all surgeons have come to accept that as a practical procedure now.

It remains to be seen whether the injection treatment of hernia will become an accepted form of treatment. It probably will in certain selected, isolated cases. I doubt, looking at it from the surgical standpoint, that it will ever supplant operation. I doubt that it will ever equal operation in efficacy, but I do think it is the sort of thing that we should all keep under consideration and keep ourselves posted on the progress made so that we will not suddenly wake up at some future date to find ourselves hopelessly behind the times, with our ideas completely outmoded.

Dr. F. W. Fiedler, Memphis, Tenn.—I met with somewhat the same difficulties in developing a clinic for this method as have been reported by Dr. Koontz. I feel that this should be the case, because in all new treatments if organized medicine does not lead in protecting the public, who will? Apparently this treatment, which is considered new by the laity, has remained in the hands of organized medicine. So long as it does, I do not think it will be exploited. It calls for more surgical technic than can be used by the cults, and consequently it will probably remain a part of our therapeutic armamentarium.

I have not had so much experience with different solutions as Dr. Koontz reports, having used only two. In my first series of sixty-seven cases, I used "sylnasol," which you know to be a sodium salt of psyllium seed oil. Since I reported that series in 1937, I have been using "proliferol T-special." In that series in which I reported 30 per cent of failures, I had attempted all types of hernia, including the direct, umbilical and incisional. My observations with "sylnasol" lead me to believe that in some individuals this chemical did not irritate the tissues sufficiently to bring about a reaction, it apparently having been absorbed like any oily solution. I find that "proliferol" will bring about a greater reaction in smaller amounts, and I think this to be an advantage.

When patients present themselves for treatment, I explain to them that the injection method has no advantage over surgery. Then I explain to them the requirements for this treatment and what they are to expect. Since it is a new treatment so far as the laity is concerned, like all new treatments they expect it to have an advantage over anything that has heretofore been done, and when you tell them that the percentage of cures is no greater than by operation, they often change their mind about having it done.

Of importance is the number of injections required. It is doubtful that we have any way of knowing. I have given as many as twenty injections and have had cures in as few as three. I recall a case where there was a bilateral indirect hernia, one the size of a goose egg, both of which have remained cured for four years, and these in a laborer. I was unable to get the patient to return after seven injections. I have had no serious complications, have probably given three thousand injections, have had some pain which always subsides before the patient is allowed to arise.

I have had a few cases of hydrocele of the sac which, of course, were usually cured by aspiration with the injection of a sclerosing agent.

I have reason to believe the elastic type of truss is responsible for some of my failures and am now using only the hood, or some modification of it. I think the pad should be placed over the internal ring, never allowing the contents to enter the canal. This can be done only by a truss that is exerting pressure there in any and all positions. I have had no patients complain of discomfort sufficient to feel that it should be discarded.

I am no longer treating private cases unless I feel certain that I can effect a cure. This, it appears to me, limits one to the indirect inguinal type, where the musculature is firm and where the external ring is no larger than three-quarters of an inch in diameter. I do not regard the size of the sac as a factor. If the external ring is large and the hernia is of long duration, the chances are the internal ring has been pulled down so it more or less overlaps the external ring, thereby obliterating the canal.

I feel that a canal an inch or so long is essential for the best results. If we are to get a cure the sac must be obliterated at its neck, and I believe this to be the most important feature of the treatment. With the obliteration at the neck and a firm abdominal wall, the condition is as it should have been at birth.

Since the indirect hernia is certainly a congenital affair, this leaves no funicular process and no potential hernia. Of course, this will all be helped by bringing about adhesions between the transversalis and the fascia of the external oblique muscle all along the canal.

I have been able to convince myself that the external ring can be made smaller. Adhesions around and below the ring give that sensation, but I do not believe constriction actually takes place. You will see that my point of believing a sac must be collapsed before it can be cured is my reason for omitting the direct, the incisional and the umbilical type of hernia.

Some of my most grateful patients are the aged with direct hernia. The sac can be obliterated, and if they are willing to wear a truss during the remainder of their life they will be free from the discomfort of the drag on the ring and the possibility of strangulation.

You well know how much criticism has been directed toward the sclerosing method, so if it is to gain a place in surgery the failures must be few and the morbidity nil.

Dr. Koontz is correct in stating that a previously injected hernia does not offer an obstacle to operation. Soon this treatment will be on a sound basis. It certainly has a place in selected cases.

Dr. Koontz (closing).—I thoroughly agree with Dr. Finney that the injection treatment certainly does not compare with surgery in the treatment of hernia, and I doubt very much that it ever will.

To those patients who want to have the injection treatment and insist upon it, I say that we do know pretty well what they can expect and what we can do with operation. In the early indirect hernias, we can tell them their chances of a lifetime cure are pretty close to 100 per cent, and with the larger and more difficult hernias the percentage decreases, depending upon the grade of hernia.

I explain that the operative method is an established method, and we know pretty definitely what it will do. But the injection method of treatment is a new method and nobody knows what it will do over a period of years, and nobody knows what the chances of a lifetime cure will be with the injection treatment. It is going to take a long time to find out, unless we all have the experience that Dr. Imes has had of having them all recur in a very short period of years.

Now, perhaps the reason that I had good cures is that the patients had not gone on long. I do not know. Another thing is that I probably used a better solution, because some that I have used were decidedly better than others. I did not get anything like such good results with the early solutions used as with the "proliferol T-special" which Dr. Fiedler has mentioned.

"Proliferol" started out as a fraction of 1 per cent of tannic acid with a few other vegetable compounds, a sort of secret formula that was gotten out by the University of Minnesota. Then "proliferol-B" came out, an improvement. Then came the "T-special," which is a combination of the old "proliferol-B" with alcohol, phenol, and other ingredients, and it is certainly much better than the first solution.

In some of these cases the early results were very encouraging. When I started out I thought, "This is certainly fine, because most of these people one can cure absolutely." And the tissues do feel perfectly strong; but the discouraging part is that a lot of tissue disappears, and in a few months it is not so strong, and in many cases there are recurrences.

The treatment, I think, will have to be much more drawn out and cover a longer period of time than has been assumed in the past if the method persists and becomes an established, accepted one. When the first strong closure is obtained, it will have to be followed by other strengthening injections. I think it will be worked out in time.

Some hernias cure themselves spontaneously; cure themselves and stay cured. Now, if some are cured spontaneously and stay cured, it is reasonable to suppose that injecting some proliferating solution will help toward the chance of a spontaneous cure, and I think you will find that you will be able to cure some cases permanently. How many, I do not know, and I do not think anybody else does.

Dr. Fiedler spoke of the individual variation which we know occurs in almost everything, and it is certainly true in these cases, because some are cured quickly with a few injections and others require many injections. There are all sorts of uncertain factors that are not settled. It will take a long time to settle them, but I think there is some place for this treatment. How much it is very difficult to say at the present time.

MENTAL SYMPTOMS IN FRONTAL LOBE TUMORS*

WITH SPECIAL REFERENCE TO THE ROLE OF THE PSYCHIATRIST IN DIAGNOSIS

By GILBERT C. ANDERSON, M.D.
New Orleans, Louisiana

In pleading for a closer cooperation between psychiatrist and surgeon I do not wish to imply that this cooperation does not already exist. It does. But it should be much more intimate than it is. It cannot be denied that when psychoses develop in the course of surgical treatment the surgeon is likely to call upon the psychiatrist more promptly and more frequently than the psychiatrist calls upon the surgeon when the circumstances are reversed. The reason is obvious. Psychoses which occur in the course of surgical treatment are usually of an outspoken nature and are promptly recognized as such, whereas surgical conditions which may occur during the course of a psychotic episode or may actually initiate it may be so masked by the psychic phenomena as to be difficult, or even impossible to recognize.

Any sort of surgical disease may, of course, occur simultaneously with any sort of psychiatric state, but certain diseases, in the nature of things, are rather more likely to occur than others. Brain tumors, and particularly tumors of the frontal regions of the brain, are such an important illustration of this fact that I propose to confine my discussion entirely to true neoplasms of these special areas. It would be well to point out, however, that the tumor (using the word in the broad sense of any swelling) may be a granuloma of luetic or tuberculous character, or an abscess, and that the clinical picture would be the same as the picture of true neoplastic disease. Such a picture might also arise on a vascular basis and be due to hemorrhage, thrombosis or arteriosclerosis. It might, finally, be due to a lesion at some distant point.

INCIDENCE OF BRAIN TUMORS

Although the statement is rather generally made that many patients are confined in institutions for the insane when their primary pathology is really brain tumor, the percentage of such

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*From the Department of Surgery of the School of Medicine of Louisiana State University.

cases is actually small. Fisher,[1] for instance, found one such case in 318 autopsies, Lubuscher[1] four in 350 autopsies, and Blackburn[1] 29 in 1,642 autopsies. Jameison and Henry[2] found 26 brain tumors (four of which involved the frontal lobe) in a study of the material collected over a 30-year period from the state institutions about New York. It is not clear that these cases represent all the brain tumors which occurred among these patients, but the inference is plain that they were all which were verified by autopsy, and the study may therefore be considered as representative. The New York State Hospital Commission, over a five-year period, found only 148 cases of brain tumor in 241,803 patients in psychiatric institutions, an incidence of about 0.6 per cent.[3] Such studies as that of Knapp,[1] who found 104 brain tumors in 5,069 mentally normal individuals, suggest that the incidence of brain tumors among the insane is actually rather lower than among the general population. The percentage of brain neoplasms located in the frontal lobe is variously reported. Two hundred sixty-two of the 1,545 tumors reported by Gibbs[4] were located in this region, as were 73 of the 239 tumors reported by Moersch,[5] and four of the 26 tumors reported by Jameison and Henry.[2]

MENTAL SYMPTOMS IN BRAIN TUMORS

Mental symptoms are common in brain tumors, regardless of the type and location. Jameison and Henry[2] report that various observers have noted an incidence varying from 40 to 100 per cent. Andral[1] observed mental symptoms in only 12 of 73 cases and Durand-Fordel[1] in only 13 of 70 cases. Gibbs,[4] in a study of 1,545 cases, found the only mental symptoms to be irritability in 27, jocularity in 33, and drowsiness in 235. Other reports show a somewhat larger incidence. Thus Nasse[1] observed mental symptoms in 19 of 50 cases, Frederick[1] in 19 of 144, and Lebert[1] in 29 of 90, Ladame[1] in 112 of 331, and Gianelli in 323 of 558. Schuster[1] and Moersch[5] found them in 100 per cent.

Other authors make general statements on the point. Bramwell[1] and Bruns[1] both state that mental symptoms are usually present in brain tumors, and Oppenheim[1] makes the unqualified statement that there can be no gross lesion in the brain without some disturbance, greater or less, in the physical functions, and that such changes can always be found by a competent observer who has known the patient intimately before his illness.

It must be granted that the definition of mental symptoms is sometimes rather elastic. Thus Moersch included in his list such purely general psychotic phenomena as listlessness, indifference, anxiety, mental and physical let-down, dullness, mild apathy, and late stupor.

Jameison and Henry[2] emphasize the fact that organic disease which occurs during the course of a psychosis interrupts or side-tracks the psychotic state, so to speak, for a greater or less length of time. During this period the patient complains and behaves very much as would a normal person developing a similar disease. A change of this sort should therefore arouse the suspicion of an alert observer and should indicate the necessity for repeated, very careful neurologic examinations. Their observations confirm those of Knapp,[1] who found that in 79 of 104 brain tumors in insane patients the change in symptomatology was sufficient to attract attention.

FUNCTION OF THE FRONTAL LOBES

The frontal lobes are usually considered the seat of intelligence, consciousness, reason and conscience, that is, the seat of the higher mental faculties, but this concept is by no means proven nor is it uniformly accepted. The present teaching seems to lead to the conclusion that the brain functions as a single organ rather than as a collection of discrete and distinct centers. An editorial[6] in *The Journal of the American Medical Association* says:

> The more recent studies, as Howell has pointed out, have tended to modify these extreme views as to localization and to emphasize the fact that histologically and physiologically the entire cerebrum is connected so intimately, part to part, that although different regions mediate different functions, nevertheless an injury or defect in one part may influence to some extent the functional value of all other regions of this organ.

Further proof of this concept is found in a case reported by Dandy[7]. Both frontal lobes were extirpated, but the patient was left

> . . . perfectly oriented as to place, time and person; the memory is unimpaired; he reads, writes, and conducts mathematical tests accurately; his conversation is seemingly perfectly normal. Furthermore, by the excision in other cases of the left occipital lobe and the lower third of the left temporal lobe we can be sure that none of these regions is responsible for intelligence. The entire body of the corpus callosum may be split in the middle without any appreciable disturbance of function. This structure is, therefore, eliminated from participation in the important functions which hitherto have been ascribed to it.

Against this evidence must be set the innumerable reported cases in which mental changes

have been associated with frontal lobe lesions, which indicate that for the time being, at least, the former concept must continue to be accepted.

MENTAL SYMPTOMS IN FRONTAL LOBE TUMORS

Voris, Adson and Moersch,[8] who reported 314 verified cases of frontal lobe tumors, found the incidence of mental changes exceeded only by the incidence of headaches and convulsive attacks. Sachs[9] found mental changes in 21 of 25 cases, and concluded that this type of symptom was most frequent and most important. Although he somewhat modified his view in a later study[10] of 20 additional cases, he still took the position that in frontal lobe tumors mental change was equalled in significance only by facial paresis.

Kolodny[11] found psychic disturbances in 22 of 30 frontal lobe tumors. Kubitschek,[12] who found mental changes in 14 of 22 cases, stated that the site, character and location of the tumor are not so important, in regard to psychic disturbances, as is the personality make-up. In his opinion the frontal lobe is neurologically a silent area and the initial neurologic signs result from increased intracranial pressure and involvement of adjacent motor, visual and olfactory structures.

Ironside,[13] in a critical review of tumors of the corpus callosum, found mental changes very common. Tilney and Riley[14] said:

> Many later clinical observations have strengthened the conviction that the frontal and premotor areas are vested with those functions of cerebral activity necessary to the development of psychic traits which distinguish man among the other animals.

CHARACTER OF SYMPTOMS

No single mental picture is entirely characteristic of brain tumor. The range is from a mere euphoric state to wild delirium and from a slight listlessness to profound depression or catatonia. The extremes, however, are the exception rather than the rule. One is more likely to encounter milder manifestations, such as errors of judgment, confusion, indifference, apathy, disregard of responsibility, and, very frequently, loss of memory, particularly for recent events. The patients become anti-social. They neglect their personal appearance. They are dirty, unkempt and careless. They are likely to empty the bladder or the rectum without regard to time or place. They laugh at irrelevant incidents, make foolish remarks, and tell silly tales and jokes. Sachs[10] has emphasized that there is likely to be associated with these symptoms a general condition of euphoria or a complete lack of grasp of the seriousness of the situation. Very often they receive with indifference the diagnosis of their condition or the news of impending operation.

Perseveration is often noted; a word, a phrase or a sentence is repeated, spoken or written, or some act is executed repeatedly, as if in a semi-automatic manner. It seems that the mind, once launched upon some train of thought, cannot be arrested or made to deviate from it. Hallucinations are not usual. Visual hallucinations are more commonly found in tumors of the occipital or temporal lobes, and auditory hallucinations in tumors of the temporoparietal regions. Olfactory or gustatory hallucinations, however, may be caused by frontal lesions pressing downward upon the tip of the temporal lobe.

Sachs,[10] as has already been pointed out, found emotional weakness of the contralateral side of the face as often as mental change. This sign is usually emotional in origin and is not necessarily the result of a deliberate voluntary muscular contraction, which makes it seem correct to consider it a mental change, similar in character to the uncontrolled outbursts of laughter and tears frequently observed in frontal lesions. Sachs' own explanation of this sign is based on his anatomic observation of the bundle of fibers passing from the cortical face center to the thalamus. No such tract, he points out, is found running from the leg or arm centers.

DIAGNOSIS OF FRONTAL LOBE TUMORS

Strauss and Keschner,[15] who made a comprehensive analysis of 90 cases of frontal lobe tumors, found mental changes in 90 per cent and observed that these changes were the first symptoms in 40 per cent of the cases. In another study with Bender,[16] they found practically the same proportion of mental symptoms in tumors of the temporal lobe, although the nature of the symptoms differed considerably. Davidoff[8] emphasizes the same difference. These authors conclude that mental symptoms, in themselves, have little or no localizing value in tumors of the brain, but that they are more frequent, more varied, and earliet in supratentorial tumors, and that complex visual and auditory hallucinations are more frequent in temporal lobe tumors.

Imburgia,[18] who considers that mental symptoms play only a small part in brain tumors, grants that loss of memory is one of the first symptoms of frontal lobe tumors. Davidoff reported two cases of frontal lobe tumors showing epileptiform convulsions and mental symp-

toms very similar to the psychic equivalent in epilepsy. Henry,[19] who made a painstaking analysis of 1,000 cases of brain tumor, found that psychotic symptoms are common in all brain tumors, but that in frontal lobe tumors they closely resemble functional psychoses and often appear before any other neurologic signs or any increase in intracranial pressure.

The experience of most neurologists is that mental changes in brain tumor have little or no localizing value in themselves, but that tumors of the frontal lobes are likely to be associated with definite changes in higher mental faculties, such as judgment, memory, social adjustment and personality, in contrast to tumors of the temporal lobe, which are likely to be associated with visual, auditory or olfactory hallucinations.

One point the psychiatrist should bear in mind is that the finding of syphilis by studies of the cerebrospinal fluid does not necessarily exclude tumor. The patient with syphilis may also have a brain tumor, which is not necessarily a gumma. Furthermore, Moersch[20] has shown that positive cerebrospinal fluid findings may occur in patients with brain tumors in whom syphilis cannot be proven. Under such circumstances it is clearly the responsibility of the psychiatrist to conduct a further exploration into the etiology of the mental changes present rather than to conclude at once that they are syphilitic in origin.

THERAPY

The diagnosis of brain tumor, or, to put it more correctly, the suspicion that a brain tumor may be present is the responsibility of the neuropsychiatrist, whose problem is to determine, as has just been mentioned, the etiology of the mental changes which form a prominent part of the clinical picture. Once the diagnosis has been established, either positively or inferentially, immediate surgical consultation should be instituted. Were it possible to determine the exact histology of the supposed tumor, it might be wisest to treat certain cases by deep irradiation, either alone or in combination with simple decompression. Such exactness of diagnosis, however, is not possible in the light of our present knowledge, and the treatment of all tumors of the cerebral hemispheres must still be entirely surgical.

SUMMARY AND CONCLUSIONS

(1) If minor alterations are included, almost all patients with brain tumors may be expected to show mental changes at some time during the course of their disease.

(2) Tumors of the frontal lobes are more likely to be associated with definite mental changes than are tumors situated elsewhere except tumors of the corpus callosum, which are almost without exception associated with such changes.

(3) The symptoms and signs of such tumors may be masked in the insane by the established psychosis, but their existence can usually be suspected if the possibility be kept in mind. The incidence is probably no greater among the insane than it is among the normal population.

(4) An important diagnostic consideration is the fact that an organic brain lesion which develops in the course of an established psychosis is likely, to a greater or less degree, to interrupt the psychosis and to simulate a like condition in a normal individual.

(5) Once the diagnosis of tumor of the cerebral hemisphere is made or suspected by the psychiatrist, surgical consultation should be sought. The treatment at the present time is entirely surgical.

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DISCUSSION (*Abstract*)

Dr. D. C. McCool, Memphis, Tenn.—Both modern psychiatry and neurosurgery have come along so rapidly in the last twenty-five years that men in those specialties have scarcely been able to digest all the developments in their respective fields, let alone keep abreast of each other's problems. And the result has been that each has tended to depend upon itself rather than to collaborate with the other. After all, neurology is the parent science of which psychiatry and neurosurgery are but branches. In pleading for closer cooperation between the two specialties Dr. Anderson has chosen a most appropriate and timely topic. It is appropriate because it has been elaborated before a joint gathering. It is timely in view of the recent interesting developments in neurophysiology, particularly the investigation of the role and function of the hypothalamus.

The organic psychoses, especially those due to frontal lobe tumors, serve as a challenge to the diagnostic acumen of every neurologist, irrespective of his specialty. It is perhaps fair to say that all psychoses due to organic brain disease have certain features in common, regardless of the type of lesion present, and that these features are even more similar as identical areas are involved. Disorientation, confusion, memory and retention defects, impairment of judgment, deterioration of moral and social conduct, and mood changes are to be found in part or *in toto* in organic psychoses. That such symptoms may be produced by frontal lobe or corpus callosum pathology primarily seems generally agreed and is not in conflict with the current concept that the brain functions as a unit.

Certain psychological criteria tend to differentiate psychoses due to frontal lobe and corpus callosum tumors from those due to cerebral arteriolar sclerosis, central nervous system syphilis, Pick's disease or Alzheimer's disease. In the former group delusions are not the rule, and with the exception of temporal lobe tumors or frontal tumors compromising the olfactory pathway, hallucinations are infrequent. Especially are auditory hallucinations unusual in tumor psychoses. Likewise the mood of a patient with brain tumor is more apt to be one of constancy and consistency. Stupor is more often an accompaniment of frontal lobe destruction. And, as Sachs and Bailey have pointed out, facial weakness on the opposite side is definitely suggestive of a neoplasm.

However, one must keep in mind that neurologic and psychological symptoms can be very misleading, for which reason caution and thorough study must be our rule. Despite careful investigation, there are times when a diagnosis is uncertain, when there are signs and symptoms present which cannot be adequately explained. It is in such cases as these that the psychiatrist and the neurosurgeon need each other. No doubt as time passes the neurosurgeon is thinking more in terms of the personality of his patient and how it is affected by the existing or suspected disease. Likewise, the psychiatrist is thinking more in terms of organic neuropathology, and no doubt these trends will soon lead to a better common understanding, a mutual interdependence, and to greater accomplishments in neurology.

Dr. Cobb Pilcher, Nashville, Tenn.—A point of particular interest in this connection, I believe, is that about 50 per cent of frontal lobe tumors are of the benign type, either meningiomas or astrocytomas, and it is patients with these slowly growing tumors who are more likely, I believe, to consult the psychiatrist. For that reason, the necessity for cooperation is more pointed than ever.

The physiologic basis of the symptoms of frontal lobe tumors is too complicated to go into in great detail here. I think attention should be called, however, to the important experimental work of Fulton and his collaborators.

In the higher primates one prefrontal lobe may be removed without producing appreciable impairment of intellectual function. On the other hand, the removal of both prefrontal regions invariably produces intellectual impairment. It has long been known that one frontal lobe may be amputated in man or that a large frontal lobe tumor may exist in man without producing mental symptoms, although it is perfectly true that most frontal lobe tumors are accompanied by mental symptoms. The fact that some tumors, therefore, do produce mental symptoms is still an unexplained mechanism. It seems likely that such symptoms are of irritative rather than destructive character.

Dr. Carrol C. Turner, Memphis, Tenn.—Dr. Anderson called our attention to the coexistence of tumors in syphilis. Recently we had occasion to see two such cases. One had had a history of syphilis and prolonged treatment with positive serum test. The patient was sent to the hospital for hyperthermic treatment. As soon as he was put in the hypertherm he developed a left hemiplegia; he had a large right frontal tumor. The second was sent for malaria therapy with a diagnosis of paresis. His serum test was positive. Just prior to his admission he developed a tumor of the right parotid gland and a week later he developed a right hemiplegia. Necropsy showed multiple melanomata, melanoma of the parotid and melanoma of the left frontal lobe.

Dr. W. de Guiterrez-Mahoney, Nashville, Tenn.—It was my good fortune a few years ago to study a series of epidermoid tumors, so-called pearly tumors, or cholesteatomas, and in reviewing as many of these as were to be found in the literature, which summed up to about 150 or so, it was striking that no matter where the tumor was, whether it was in the cerebellar pontine angle, where 50 per cent of them occurred, or in the fourth ventricle, or about the hypothalamus, or over the cortex, probably 75 per cent or more of the patients had symptoms of mental disorder. Historically, it is interesting that Samuel Wilks in about 1850 presented two of these tumors with the brains to a society in London and asked that they be collected over a period of years, until enough were available to investigate the question of why many of them occurred in the insane. Pathologically it is interesting, in so far as a lesion which is common to all of them is demonstrable in the nature of an encephalitis. From the clinical pictures I extended the work into the experimental field, and by putting cholesterin, which is the chemical constituent of these tumors, about the brain of animals, the same type of reaction was found experimentally, and I think here we have a chemical reaction which occurs from a specific type of tumor and is responsible for mental disorder.

Dr. Anderson (*closing*).—I tried to bring out in the

paper that tumors anywhere within the cranial cavity or, for that matter, any other space-encroaching lesion, are more than likely to cause changes in the psyche. They do not seem to be more frequent in frontal lobe tumors than in tumors of other regions, the temporal lobe tumors, for instance, when careful analyses are made, but they do seem to have a different characteristic.

OPHTHALMOLOGIC CONSIDERATIONS IN NEUROSURGICAL CASES*

By KATE SAVAGE ZERFOSS, M.D.
Nashville, Tennessee

Neurosurgery as it pertains to the removal of intracranial tumors had its modern beginning in 1902 when Cushing did his first operation. Since that date two contributions have been outstanding in advancing this work. Dandy introduced ventriculography in 1918 and electrosurgery was applied to neurosurgical procedures later, in 1926.

The demand for an ophthalmologic examination is still present and should be done preferably in advance of all other surgical procedures, not excepting the making of encephalograms or ventriculograms. The role of the ophthalmologist in this field of neurosurgery is to make his routine examinations with such care and completeness that there will be an identification of all cases in this category. Two extremes appear usually in private and clinical practice, these being the early and the late cases. Optic atrophy is often encountered in one or both eyes. These early cases invariably present themselves with a request for a refraction, complaining of headaches, eye discomfort and blurred vision of a transitory nature.

The second group is usually referred by an internist, the symptoms being more advanced than the early cases. The third group comprises the definite "tumor suspects" and is to be examined in order to confirm this opinion and to aid in the localization of the lesion. Negative findings are of value; however, the complete scope of the examination should be indicated as exclusion of certain lesions at specific sites may prove to be of importance. The time factor is to be considered as the visual fields and acuity may change abruptly in a rapidly expanding intracranial tumor.

The last group of our cases is composed of those who have had the original diagnoses made and operations done in other cities. These were followed postoperatively, as well as our own cases, to note the progress and improvement and in some instances the recurrences.

It is of value to remember that the earlier a patient with an intracranial tumor is seen the fewer and less pronounced and less typical will be the signs and symptoms. The history of each such case should be carefully taken with accurate descriptions made of the headaches especially, as well as the other symptoms. As complete a history is expected of the ophthalmologist as of the internist.

The following list indicates the major points to be checked in each examination:

(1) Headache
(2) Nausea
(3) Vomiting (projectile)
(4) Vertigo
(5) Diplopia
(6) Blurred vision and decreased acuity
(7) Choked disc
(8) Convulsive seizures
(9) Unconsciousness
(10) Mental status

In the above group of symptoms and signs one is impressed by the consistency of the occurrence of the headaches and the relative freedom from the convulsive seizures, also the preservation of vision in the early stages. Periods of unconciousness without convulsions are noted frequently.

A suggested outline for reporting as a consultant to a neurosurgeon and as a basis for routine study of all cases included in this group is as follows:

I. Visual acuity at twenty feet and at fourteen to sixteen inches, refraction correction, presbyopic correction
II. Extrinsic muscle balance
  (1) Nystagmus
  (2) Paresis
  (3) Paralysis
III. Intrinsic muscle balance
  (1) Pupillary reflexes to light and accommodation
  (2) Consensual reflexes
  (3) Size, shape and equality of pupil
IV. Fundus examination
  (1) Negative fundus and disc
  (2) Paleness of disc
  (3) Papilledema of disc, blurred margin and decrease in cupping

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*From the Department of Surgery, Ophthalmology Division, Vanderbilt University School of Medicine.

(4) Choked disc, height of elevation, one to eight diopters and retinal hemorrhages, side of greatest choking
(5) Atrophic disc, primary
(6) Secondary optic atrophy following receding of edema
(7) Size of retinal arteries and venous engorgement
(8) Exclusion of other fundus disease as glaucoma, degeneration of the retina without pigment and with small arterial caliber

V. Perimetric studies, fields of vision with interpretations
(1) Concentric constrictions
(2) Quadrant defects, right or left, superior or inferior
(3) Homonymous hemianopia, right or left
(4) Bitemporal hemianopia
(5) Complete loss of visual field with atrophy of optic nerve
(6) Altitudinal defect, superior or inferior
(7) Bizarre fields in suprasellar tumors and recurrences
(8) Binasal, rarely found

VI. Cooperation, mental status, condition at time of examination

VII. Remarks

VIII. Localization of intracranial tumor indicating site, side and type

If the patient's condition is such that one anticipates difficulty in completing the perimetry at one sitting it is advised that the examination be confined to the following meridians first: 90, 180, 45, 135, 225, 270, 315 and 0.

In taking fields of vision one finds it more convenient and also less time-consuming for the patient to place the number of degrees at the periphery of the chart and to complete the plotting later. A hand perimeter may have to be employed occasionally should the patient be too incapacitated to be seated in the upright position. The presence of a nurse, orderly or technician expedites the process as continuous observation is essential. If possible have an assistant seated on the opposite side to aid in observing and recording.

A brief outline may be used to indicate the relationship of the findings to the anatomical site of the intracranial tumor.

(1) Optic nerve	Complete blindness and field obliteration
(2) Optic chiasm	Bitemporal hemianopia or atypical fields
(3) Optic tract Visual radiations Occipital cortex	Homonymous hemianopia, right or left as to loss of field. Lesion on the opposite side of the defective field
(4) Anterior to external geniculate body	Hemianopic pupillary reaction and atrophy of fibers on disc on homonymous sides
(5) Posterior to external geniculate body	No pupillary disturbances and no atrophy of discs
(6) Optic tract	Complete damage to fibers. Homonymous field defect extending to 90 degrees
(7) Visual radiations	Macular fibers uninvolved, central vision preserved. Bilateral cortical representation of the maculae
(8) Temporal lobe, visual radiations	Homonymous quadrant defects

Some additional special considerations as pointed out by Gifford are as follows:

(I) Frontal lobe, meningiomas
(1) Direct pressure, optic nerve atrophy without papilledema, same side as tumor
(2) Papilledema of nerve on opposite side
(3) Anosmia, same side as tumor

(II) Pituitary tumor, adenomas
(1) Bitemporal hemianopia
(2) Adiposogenital syndrome, Frohlich
(3) Acromegaly

(III) Suprasellar meningioma
(1) Field defects in lower half or atypical fields as to shape of defect

Papilledema is absent in the above types of cases and atrophy is due to direct pressure.

Sachs says:

"The macula is bilaterally represented, so that a lesion of one occipital lobe or one optic tract does not destroy macular vision."

Gifford says:

"At the optic chiasm these fibers decussate in part, running uncrossed in the outer parts of the chiasm while those from the inner halves cross to the opposite inner part of the chiasm. *The papillomacular bundle undergoes the same semidecussation.*"

Since Dandy's introduction of ventriculography the ophthalmologist should acquaint himself with the x-ray plates made in stereo as well as those plates made prior to introduction of air in the ventricles. A study of these made with both the neurosurgeon and the roentgenologist gives a more complete appreciation of their interpretations.

Listed below is an outline of considerations of the points to be observed in the study of x-ray examinations as indicated by Sachs:

(1) Calcifications, generalized shadows, specific as in vessels and cyst walls
(2) Convolutional atrophy

(3) Suture separations
(4) Pressure atrophy of the bone
(5) Invasive tumors of the bone by meningiomas and endotheliomas
(6) Dorsum sellae, erosion
(7) Sella turcica, width, depth and shape
(8) Anterior and posterior clinoid processes, displacement, tilting and erosion
(9) Calcified pineal gland, displaced to opposite side by cerebral tumors
(10) Calcification of choroid plexus
(11) Diploic vessels
(12) Ventriculograms (Dandy)
  (a) Ventricles
    (1) Dilated, one or both
    (2) Displaced to opposite side and compressed
    (3) Obliteration of one horn
    (4) Obstruction of aqueduct of Sylvius or foramen of Monro

The experimental work by Clark and Ward on gradually expanding intracranial tumors is a contribution to the knowledge of the mode of production of the cerebral compressions and deformities and a valuable aid in the understanding of tumor formation.

In 1933 the neurosurgical service was reorganized and placed on a full-time basis. During this period, 1933 through October, 1940, a total of 173 cases of proven intracranial tumors have been observed. The following cases have been chosen as being representative of their respective groups. These will be summarized briefly.

Case 1.—J. W. L., a white man, aged 40, was admitted September 26, 1940. The diagnosis was basophile adenoma of the pituitary gland, recurrence. Operation consisted of ventricular puncture with air injection and cerebral craniotomy, with tumor removal. Previous craniotomy was done February 25, 1937, and x-ray therapy was administered. Fields of vision showed bitemporal hemianopia, atypical, O.D.V. 20/40 and O.S.V. 20/30. Ventriculograms showed moderate dilatation of both lateral ventricles with a midline filling defect evidently caused by a mass protruding upward in the anterior posterior view. The third ventricle was not visualized. There was no displacement of the ventricles. Postmortem examination revealed posterior extension of the tumor into the posterior fossa in front of the pons and medulla and bronchopneumonia.

Case 2.—L. J. M., a colored woman, aged 30, was admitted January 5, 1937. The diagnosis was eosinophilic adenoma of the anterior lobe of the pituitary gland with acromegaly. Operation consisted of cerebral craniotomy, with tumor removal. Fields of vision showed bitemporal hemianopia, atypical. O.D.V. was 20/40 and O.S.V. 20/50. X-ray showed acromegaly.

Case 3.—Mrs. L. R., a white woman, aged 51, was admitted October 14, 1940. The diagnosis was pituitary dysfunction with suspected tumor and inoperable. Fields of vision showed concentric constriction. O.D.V. was 20/30 and O.S.V. 20/30. There were third nerve paralysis and bilateral papilledema. Her maximum weight was 410 pounds; present weight 350 pounds.

Case 4.—Mrs. L. G., a white woman, aged 48, was admitted November 15, 1937, with a diagnosis of cystic astrocytoma of the parietal lobe. Operation consisted of ventricular puncture with air injection and cerebral craniotomy with tumor removal. Fields of vision showed homonymous hemianopia. O.D.V. was 20/30 and O.S.V. 20/50. August 17, 1938, O.S.V. was 20/200. It is now 20/40. Ventriculograms revealed the entire ventricular system was displaced to the left about 1 cm. There was a flattening of the superior margin of the right lateral ventricle. The left ventricle was only partially visualized. There was a break in the contour of the right lateral ventricle about the midportion of its body. The impression was that a lesion occupied space on the right, probably in the parietal region.

Case 5.—H. E. B., a white man, aged 38, was admitted September 15, 1931, with a diagnosis of suspected neoplasm of the brain. On January 1, 1939, the diagnosis was cerebrospinal rhinorrhea; on February 12, 1940, pneumococcal meningitis. Operation on October 2, 1931, consisted of cerebral craniotomy, exploratory, with decompression. Operation on February 2, 1932, consisted of ventricular puncture with air injection. This was repeated on December 12, 1938.

All fields of vision were atypical, with repeated changes. O.D.V. was 20/30; and O.S.V. no L.P. Ventriculograms showed an increase in the convolutional markings, absence of the floor and enlargement of the sella turcica. There was uniform dilatation of the ventricular system, the third ventricle ballooning downward into the sella actually. The fourth ventricle and aqueduct of Sylvius were dilated. The patient expired February 13, 1940. Autopsy was refused.

Case 6.—Miss J. O., a white girl, aged 16, was admitted June 20, 1939, with a diagnosis of congenital hydrocephalus and atresia of the aqueduct of Sylvius. Operation consisted of ventricular puncture with air injection; exploratory cerebellar craniotomy and cerebral craniotomy with removal of the choroidal plexus. The fields of vision showed slight concentric constriction. O.D.V. was 20/20 and O.S.V. 20/20, with choked discs. Ventriculograms revealed marked convolutional atrophy, separation of sutures, sella flattened and posterior clinoid processes almost completely obliterated. There was calcification of the pineal gland with no displacement, and a huge, uniform, symmetrical dilatation of both lateral and third ventricles without displacement or deformity. The aqueduct and fourth ventricle could not be demonstrated. The condition seemed to be an early stage of acromegaly.

Case 7.—J. W. H., a white boy, aged 17, was admitted July 29, 1938, and readmitted June 11, 1939. The diagnosis on September 29, 1938, was astroblastoma with cyst formation in the fronto-parieto-temporal region. The second admission was for a recurrence. Operation August 4, 1938, consisted of ventricular puncture with air injection and cerebral craniotomy with tumor removal. On June 21, 1939, cerebral craniotomy with secondary tumor removal was done. The fields of vision showed homonymous quadrant defects, right upper nasal and left upper temporal. O.D.V. was 20/20 and O.S.V. 20/20. Ventriculograms revealed considerable dilatation of the

diploic vessels. The posterior clinoid processes showed a little thinning. There was slight convolutional atrophy in the middle fossa. The entire ventricular system was displaced to the left. There was partial obliteration of the posterior horn of the right ventricle due to a tumor located posteriorly on the right side. X-ray therapy was administered.

Case 8.—G. S., a colored girl, aged 12, was admitted October 20, 1939. The diagnosis was calcified hemangioma of the right occipital cerebral cortex; osteomyelitis of the occipital bone (bone flap), and osteomyelitis of the parietal bone (bone flap). Operation consisted of cerebral craniotomy with tumor removal and amputation of the right occipital lobe, posteriorly and medially. The postoperative fields of vision revealed left homonymous hemianopia with O.D.V. 20/30 and O.S.V. 20/30. Roentgenogram of the bones of the skull showed no evidence of defect. An irregular, wavy calcification was seen in the lateral view which in the anterior posterior view was just to the right of the midline. A large, patchy calcification showed linear markings and seemed to follow the course of some vessels. It was believed that this represented an angioma with calcification.

Case 9.—Mrs. J. W. H., a white woman, aged 26, was admitted July 29, 1940, with a diagnosis of parietal lobe meningioma. Operation consisted of ventricular puncture with air injection and cerebral craniotomy with tumor removal. Ventriculograms revealed an increase in the convolutional markings in the frontal fossa; displacement of the ventricular system to the right and flattening of the superior surface of the posterior portion of the body of the left ventricle obviously by a mass lying above the ventricle near the midline.

Case 10.—E. C. K., a white man, aged 36, was observed first on January 2, 1932. The diagnosis was meningioma of the right fronto-parietal region. Operation on March 18, 1931, consisted of craniotomy with removal of the meningioma. Operation November 11, 1932, consisted of craniotomy with removal of a meningioma recurrence. The fields of vision showed bitemporal hemianopia. O.D.V. was 20/20 and O.S.V. 20/100; O.D.V. was 10/15 and O.S.V. 10/40; August 1, 1932, O.D.V. was 5/40 and O.S.V. 5/200; December 18, 1935, O.D.V. was 20/40 and O.S.V. 20/50; March 23, 1938, O.D.V. was 20/30 and O.S.V. 20/25; October 23, 1940 (macular sparing), O.D.V. was 20/30 and O.S.V. 20/30. Roentgenograms October 23, 1940, revealed a large defect in the right fronto-parietal region, the result of previous craniotomy. The patient had nocturnal convulsions December 14, 1939, and March 9, 1940.

Case 11.—B. F. R., a white boy, aged 11, was admitted July 13, 1940. The diagnosis was encapsulated abscess of the right parieto-occipital lobe region, and tumor was suspected. Operation consisted of ventricular puncture with air injection; craniotomy and drainage of abscess, 50 c. c. being aspirated; and drainage of the abscess and hematoma, 20 c. c. being aspirated. The fields of vision revealed left homonymous hemianopia, loss of central vision, and bilateral papilledema. On November 1, 1940, he showed complete recovery from the field defects. Ventriculograms revealed the entire ventricular system displaced to the left, with encroachment on the lateral wall of the right lateral ventricle. The posterior horn of the right lateral ventricle was markedly compressed. The impression was of a large mass on the right side, probably in the middle fossa of the temporal lobe.

Case 12.—Mrs. E. T. F., a white woman, aged 47, was admitted February 25, 1937. The diagnosis was perineural fibroblastoma of the right eighth nerve, and optic atrophy due to pressure. Operation consisted of cerebellar craniotomy with tumor removal in two stages, March 5 and March 15, 1937. Fields of vision were not obtainable. There was optic atrophy and marked papilledema. She had previously experienced hallucinations of vision. Ventriculograms revealed a considerable dilatation of all the ventricles without displacement. Hydrocephalus but no tumor was seen. The patient is living and well. Optic atrophy exists to the present date.

In the scope of this paper, which is necessarily limited due to the extent of the subject chosen, particular stress has been placed in the study of the fields of vision and the ventriculograms.

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DISCUSSION (*Abstract*)

Dr. Grady E. Clay, Atlanta, Ga.—Dr. Zerfoss stresses the importance of early recognition of ocular symptoms seen in practically all neurosurgical cases. Unfortunately many of the cases seen by the neurosurgeon have first been seen by the ophthalmologist who has failed to recognize even the late symptoms.

One of the most frequent errors of the ophthalmologist is the early recognition of chiasmal lesions. The author failed to mention the occurrence of a retrobulbar neuritis in this group as a not uncommon early symptom, and it is these cases which are often overlooked until an atrophy begins to develop in the other eye. Such a case early may have a normal fundus with a central scotoma without any temporal defect. Surely when such a case begins to show a slight temporal defect there can be no question of a chiasmal lesion, even if

the other eye is normal in its fields, and if all other findings are negative we should advise an exploratory operation before a primary optic atrophy does develop. In such cases we should keep in mind that chiasmal subarachnoiditis may produce the same findings. Therefore, in every case of retrobulbar neuritis, whether unilateral or bilateral, one should first suspect a neighborhood chiasmal lesion.

A retrobulbar neuritis presents only one picture, namely: a normal fundus with usually a central scotoma, and in any such case when the nerve head becomes swollen the disease then is no longer a retrobulbar disease, but becomes an optic neuritis.

An optic neuritis with a central scotoma is not a rare occurrence. It is seen in many of the encephalitides and especially in the demyelinizing diseases, most common in neuromyelitis optica. There is a group to which I should like to call your attention, occurring most frequently in children from 6 to 18 years of age, during the late summer months. The child suddenly goes blind with a central scotoma, having slight peripheral fields intact, and on the following day the same symptoms occur in the other eye. This rapidly progresses to blindness without the occurrence of any other symptoms. The only positive finding is a very marked swelling of the optic nerve head, usually 4 to 6 diopters; the swelling is often similar to that of a choked disc. Such a group of diseases we feel sure is due to a virus infection and the optic nerve disease emulates that seen in neuromyelitis optica.

Subdural or subarachnoid hemorrhage cases are neurosurgical and should not be overlooked. The eye findings are frequently positive and present a marked choking of the disc with hemorrhages over the nerve head and into the retina, so profuse at times that they may extend into the vitreous, and such a picture is diagnostic.

Lastly, in considering neurosurgical lesions, one should not overlook hysteria, and the still more common mistake of calling a pseudo-optic neuritis or drusen bodies of the disc a choked disc and subjecting such cases to craniotomy.

Dr. Cobb Pilcher, Nashville, Tenn.—Since the superb work of Walker, working in collaboration with Dr. Cushing years ago, the neurosurgeon has recognized even better than the ophthalmologist the extreme importance of careful perimetry in the localizing of cerebral tumors. Perimetry, I think, offers the nearest approach to mathematical exactness in the field of localizing neurologic diagnosis, and careful determination of the visual fields is an integral part of the neurologic examination.

Dr. B. Y. Alvis, St. Louis, Mo.—Frequently the first signs of intracranial tumor are found by the ophthalmologist. Too frequently they are not recognized as possibly being signs of intracranial tumor.

The importance of ocular signs in the diagnosis of brain tumor was summarized by Dr. Ernest Sachs, of St. Louis, in an address before the American College of Physicians in 1937. He divided these signs into five groups: ocular palsies, ocular movements, visual defects, ophthalmoscopic changes and subjective visual disturbances.

The most important ophthalmoscopic finding in a brain tumor case is choked disc. This must be differentiated from optic neuritis, which is not always easy in the early stages. An important differential point is the vision which is usually normal in early choked disc, but impaired early in optic neuritis.

Optic nerve atrophy may be due to a brain tumor in the chiasmal region.

In an article by Dr. Leo Mayer, of Chicago, in the *Archives of Ophthalmology* of February, 1938, there appears a diagram which illustrates graphically the visual field changes corresponding to lesions affecting the visual pathways at various points. This chart is most helpful in refreshing the memory as to the possible location of the lesion producing a given type of field defect.

The quadrant defects are not necessarily indicative of early tumor, but are valuable localizing signs pointing to temporal lobe lesions.

Dr. Clay mentioned the fact that intracranial tumor may produce symptoms and signs simulating retrobulbar neuritis. A case we saw a few years ago illustrates this point. This lady, aged about 40 years, complained of lowered vision of the left eye and severe retro-orbital headache on this side. The disc was essentially normal, the field changes variable. No other neurologic signs were made out. For many months no definite diagnosis could be made and it was thought the symptoms might be of neurotic nature. Finally the region of the chiasm was explored and a tumor removed, relieving her pain and checking the progressive loss of vision.

The eye physician frequently has the first contact with the brain tumor case. He should be alert to detect the early symptoms and call on the neurosurgeon for help in suspected cases without waiting for the signs to become obvious when it may be too late.

THE TREATMENT OF FRACTURES OF THE SHAFT OF THE HUMERUS*

By DUNCAN EVE, M.D.

and

ROLLIN A. DANIEL, JR., M.D.

Nashville, Tennessee

The successful treatment of fractures of the shaft of the humerus has in the past presented difficulties which are today reflected in the many and varied methods of procedure recommended in the literature on this subject. It is not the purpose of this paper to add to any confusion which may exist, but rather simply to present a group of cases which has been treated satisfactorily by one method. The method itself is not new, but its detailed description is justified because of the continued use of open reduction and internal fixation.

At the present time methods of treatment are based, for the most part, on two distinct ideas. The first is the reduction of the fracture and the

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maintenance of reduction by immobilization. The second is the accomplishment and maintenance of reduction by the use of traction.

The latter principle has received much attention during the last few years through the common use of the so-called "hanging" or "traction" cast, first suggested by Caldwell[1] in 1933 and advocated since then by Griswold[2] and others. In 1939, Griswold reported 68 fractures of the shaft of the humerus treated by this method with only one nonunion and with good results in the remainder. It has the advantage of ease in application and the disadvantages that the extremity is not immobilized and that the patient must be in the upright posture for the proper maintenance of traction. Its use is admittedly limited to those patients who are able to remain upright, or nearly so, even during their sleeping hours, at least during the early period of their treatment. As has been repeatedly emphasized by Griswold, the hanging cast will not reduce a fracture above the insertion of the deltoid muscle, and will control these only if they are properly reduced and if, as is usually the case, the long head of the biceps is intact.

Traction by means of a rope and pulley, applied either to a pin through the olecranon or to a Buck's or adhesive dressing, is widely used. If care is taken not to abduct the arm too markedly, such an appliance will usually suffice if other conditions, which require the patient to remain flat in bed, are present.

A dressing which splints the arm directly against the chest wall is occasionally used. The maintenance of reduction is extremely difficult with such an appliance. Recently Gurd[3] has described a plaster cast which is a modification of this type of dressing, and which overcomes many of the objections to it. A firm triangular pad is inserted into the axilla, which places the arm at about 15 to 20° of abduction. A plaster cast is then applied which covers the shoulder and the arm, encircling the chest. Just before the plaster hardens it is moulded to the anterior and posterior surfaces of the arm in such a way that two gutters are made between the arm and the axillary pad. The elbow and forearm are left free and the elbow is maintained at a right angle by means of a sling applied at the wrist. It is felt by Gurd that immobilization of the shoulder joint and the moulding of the plaster to the arm keep the fragments in better alignment than is possible with the hanging cast, especially with the patient in the recumbent position.

Many writers have compared fractures of the shaft of the humerus with fractures of the shaft of the femur. This has been done by advocates of the hanging cast, and this method of treatment has been compared with the use of the Thomas splint in the treatment of fractures of the femur. We feel that such a comparison is not correct, and in many instances bespeaks a lack of knowledge of the principles involved in the proper use of the Thomas splint. The fragments of the femur can be controlled and immobilized with the Thomas splint, whereas this cannot be accomplished in the case of the humerus without either the use of strong traction, which is not desirable, or rigid immobilization of the shoulder joint.

Strong traction is not required for the reduction or the maintenance of good position in fractures of the shaft of the humerus. The occurrence of nonunion is fairly common, and in these respects the humerus can be compared to the tibia. Immobilization of the knee and of the ankle in fractures of the shaft of the tibia is generally practiced, and probably would continue to be done even if it were possible for the patient to carry the leg in a dependent position and without bearing weight, as is the case with the arm. Immobilization of the shoulder joint with fractures of the shaft of the humerus would seem to be as important, both because of the expectation that union might occur more quickly as well as to avoid further trauma to the soft tissues and possible injury to the musculospiral nerve.

The plaster shoulder spica cast has been used by us in 35 consecutive cases. All have been private patients. Approximately two-thirds have been treated in the office and the remainder in the hospital. A few have received treatment without anesthesia; the majority have had local anesthesia, five to ten c. c. of 1 per cent procaine hydrochloride solution having been injected into the hematoma. The ages of the patients have ranged from 8 to 64 years. Sixty-three per cent were fractures of the middle third of the shaft, 25 per cent of the upper third, and 12 per cent of the lower third.

Two patients received injuries to the musculospiral nerve at the time of the accident. No patient showed any evidence of injury after treatment was instituted and complete nerve function returned in the cases mentioned above.

Open reduction was performed upon one of the patients, in which there was a long spiral fracture in the middle of the shaft, the ends of

the fragments becoming embedded in the muscle and preventing reduction. The cast described here was applied after operation.

There were no cases of nonunion in this group and good functional results have been obtained in all of them, firm union being obtained in all cases by the end of a period of 8 to 10 weeks.

The method of application of the cast and the care of the patient are briefly summarized as follows:

The patient is placed on a stool in the erect sitting position. The operator, with one hand grasping the elbow and the other supporting the hand, applies moderate traction to the arm. The arm is held in a position of from 20 to 35° abduction with the elbow slightly forward and maintained at a right angle. This amount of abduction is sufficient to relieve the pull of the supraspinatus muscle and to permit moderate relaxation of the deltoid. The not uncommon shoulder joint complications associated with contracture of the abductor muscles, and subdeltoid and subacromial inflammatory reactions, are not encountered if this is done. The forearm is held in mid-pronation and the wrist in extension. The circular cast is applied down to the wrist, a plaster splint being incorporated in the axilla and a light splint being extended under the palm to support the hand.

Following reduction, the patient is permitted to resume any activity which he feels he is able to pursue. He is encouraged to exercise his wrist and fingers, and after about 3½ weeks the "roof" of the cast covering the extremity is removed and thereafter passive motion of the shoulder and elbow is instituted. The entire cast is removed at from 4½ to 5½ weeks, depending upon the type and location of the fracture and the age of the patient.

During the first two or three days following reduction and application of the cast, occasional patients have complained because of the weight of the cast. In all cases, after this period of "adjustment," patients have been comfortable. In most cases, reduction has been accomplished satisfactorily with the first operation, but in a few instances x-ray examination following application of the cast has revealed an unsatisfactory position of the fragments. In these cases, the cast has been removed, the alignment of the fragments corrected and the cast reapplied. It is better in these cases to remove the cast completely, and reapply it, than to try to correct the deformity by removing a part of the cast and attempting to "patch" it.

After removal of the cast, the patient is instructed to exercise the extremity by the use of an overhead pulley and by the use of rotary swinging motion of the shoulder joint. Complete return of normal function varies with different individuals, but is usually complete within twelve weeks after receipt of the injury.

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DISCUSSION (*Abstract*)

Dr. H. Earle Conwell, Birmingham, Ala.—Dr. Eve has very ably presented a subject which has recently become very controversial. If I had been asked my opinion ten years ago as to the most frequent site of nonunion in fractures, I would have said the lower third of the tibia. Today, however, it is my opinion that this location has changed to the middle two-fourths of the humerus. The type of treatment for a fractured humerus depends upon the location of the fracture just as in the femur or any long bone. We seldom see a nonunion of the upper or lower thirds of the humerus which has originally been properly reduced.

The majority of nonunions of the humerus occur in the middle two-fourths and it has been my experience that 75 per cent of these are transverse fractures. It is easy to see why the transverse fracture most frequently develops nonunion, because of the difficulty of maintaining a good position. It is here, mainly, that the advocates of the hanging cast maintain that they have a better method of treatment. Personally, I feel that the hanging cast goes against all principles of fracture treatment and repair. However, good results have been obtained with it in experienced hands. Even the enthusiasts warn against the indiscriminate use of the hanging cast by those who are not familiar with the do's and don'ts of its use. When I see the results which have been obtained by experienced surgeons who have used the technic I cannot help but believe in them. I am still mainly an advocate of rest and immobilization in the treatment of humerus fractures, because it fulfills the main principles of the treatment of all fractures which were emphasized by Hilton and Hunter many years ago, namely, rest and immobilization.

I was pleased to hear Dr. Eve emphasize the importance of not getting too much abduction in the humerus fracture, and also to hear him say that strong traction is not necessary. Not more than 5 per cent of nonunions in fractures through the middle two-fourths of the humerus has been encountered in my cases and such a complication in my series could not always be attributed to poor position, because most of the cases originally had severe local trauma which always has to be taken into consideration in fracture treatment.

The initial treatment of severely damaged humeral fractures should be stressed. Dr. Eve, I know, desires it to be thoroughly understood that such fractures cannot be treated with a cast until the compound wound or severely traumatized tissues have improved sufficiently

to warrant it. Fortunately, however, such injuries make up a very small per cent. The difficulty or the ease of reduction of any fracture, be it the humerus or another, is generally in direct relationship to its original displacement, and therefore it is in direct proportion to the difficulty of maintaining reduction.

Dr. J. Albert Key, St. Louis, Mo.—I think Dr. Eve's is a good method. I have used it myself. It took me three or four years to get around to the hanging cast. It will not solve the problem presented by every fracture of the humerus, but one is surprised to find what a large percentage of them it will solve.

I saw no fractures on the screen which could not, I believe, have been treated successfully with a hanging cast. Also, the patient would have been much more comfortable during convalescence than he would had I put on a plaster spica of the shoulder, such as I am in the habit of using and have used in the past.

It is very difficult to apply a comfortable spica to the shoulder which will be efficient.

With a hanging cast I sometimes let the patient stay in bed for a day or two and tie a bandage onto the cast so that the knot is posterior to the elbow; then run it over the foot of the bed and hang on a weight of five or eight pounds, leaving the forearm across the chest. That makes it as comfortable as the patient is when he is up.

Give the patient a week with the hanging cast before you get an x-ray. Do not expect the hanging cast to reduce the fracture in twenty-four hours. In my experience, most of them by the end of the week are in a satisfactory position. If they are not, the cast can be wedged or you can displace one fragment laterally.

You can partly control the lower fragment by pronation or supination of the forearm.

I disagree with Dr. Eve that where you use the spica it is easier to put on a new spica than it is to correct the position. In my experience, after I get the spica on and find the position is not satisfactory, I can get a satisfactory position with much greater ease by wedging the cast or cutting the cast and displacing one fragment laterally and then splicing it together with a plaster bandage than by starting all over again.

When I start all over again, I usually have about the same luck that I had the first time; but by wedging or displacing it laterally, I have much better results. Then, if the hanging cast is not successful, I can resort to a spica. Or, if the situation is such that I can do it with safety, I do an open reduction.

The great majority of these cases can be treated successfully with the hanging cast, and the hanging cast gives more comfort to the patient and much less trouble to the surgeon.

Dr. F. Walter Carruthers, Little Rock, Ark.—The type and method of treatment that should be used depend upon the location of the fracture. If I understand anything about the hanging cast, it is this: when Dr. Griswold showed these cases in Louisville several years ago at the Clinical Orthopedic Society, I think he astounded most of us who were present. We asked him, "Doctor, did you use that in the middle third of the humerus?" and he said he did.

We were a little leery of it, but he treated about twenty-five cases, I think, and showed about twelve under treatment at that time. Dr. Conwell will remember that.

My use of the hanging cast has been around the surgical neck of the humerus, not in the shaft. I am a little leery of using a hanging cast in the middle third of the humerus, but I have surprised many a patient and also many a physician who has referred the case to me for treatment by using a hanging cast.

I have an old lady in the hospital now with a fracture of the pelvis which I reduced about a week ago. She reminded me, "Do you have to put a cast around my pelvis?" and I said "No."

She said, "I'm glad, because I remember you treated Mrs. Jones with a fracture of the neck of the humerus without having to put any body cast on, and she got perfect results."

The other thing which should be emphasized about the shaft fracture is the necessity for very little traction. You can put on too much traction. We all talk about the necessity of applying traction in the treatment of fracture, but it takes very little traction to handle a fracture in the shaft of the humerus. You will be surprised to see how little it does really take.

In order to make the matter safe, I think, you can apply traction with the use of adhesive and then turn it back and incorporate it into the cast. You can feel pretty sure that it is going to stay. Check up with the fluoroscope and also with an x-ray afterward.

Also, in many types of fractures, you can insert a pin in the lower end and maintain adequate fixation with a pin incorporated into the cast.

Dr. Abbott at Des Moines, I believe, recently circulated a reprint on the use of Russell traction in treatment, but in my country money is scarce, and we have to try to get people out of the hospital as soon as possible.

We are still operating under the New Deal, and economics is still a paramount issue in Arkansas. I do not know whether that is true in Alabama, but it is in Arkansas, so if we put a Russell traction on these patients, and keep them in the hospital for six or eight weeks, the physician has nothing and the hospital has to keep them in for nothing during the last two weeks, and so, all in all, my opinion is that it all depends upon the patient, upon the conditions existing, and upon the type of fracture as to what treatment we are going to use.

Then there is the question of nonunion. I used to think nonunion in the lower third of the tibia was outstanding. I have become more and more convinced that it is a question of nonunion of the humerus. Dr. Burns' method of posterior bone grafts on these cases, which I used not more than a week ago, I think is a great contribution so far as bone graft is concerned in the treatment of nonunions.

Dr. R. Arnold Griswold, Louisville, Ky.—All of us who are treating fractures of the humerus are beginning to get at the same center from different points of the compass, Dr. Eve coming from one direction and those of us using the hanging cast from another.

This is an extremely interesting problem, and we feel that the hanging cast has solved many of our problems in connection with fractures of the shaft of the humerus. The hanging cast is not foolproof, and it is not a panacea for all ills, but it does work.

Someone has said that every time he puts one on and sees that it works he is surprised, but he uses it. I feel somewhat the same way. However, it does not work in every condition. This morning up at the City Hospital Dr. Kelly, the resident in orthopedics, is doing an open operation on a humerus. The patient came in last week with a transverse fracture of the shaft. A hanging cast was put on it. It was x-rayed a few days later and it was not together. There must have been some displaced muscle between the fragments, so he is opening the arm this morning and taking the muscle out from between the fragments, but he is putting it back in a hanging cast.

There are many theoretical objections to this method of treatment. Several years ago when we first started, a good friend in Louisville called me up and said, "You have an intern at City Hospital who is a fool. I have a patient who was treated there for a fractured humerus and the cast does not even come to the fracture. I called the intern and he said that it was the right way to do it." I started trying to convince the fellow that it was right, and by the time I got through he thought I was a fool, too. Now he is using the method.

Dr. Lloyd J. Netto, West Palm Beach, Fla.—Fracture of the humerus has always been a difficult problem because there are many different types of apparatus, ranging from the airplane splint on down a long confusing list.

I want to rejoice at the fact that the men in the big centers who are doing a lot of fracture work are having as much trouble, at least, in agreeing upon methods, as we are. In my section of the country we must consider the comfort of the patient a little more than elsewhere, because it never gets colder than about 60 degrees in Florida, so the spica that Dr. Eve taught me to use some years ago, while I think it is a good method for the average man and I have used it a great deal, is difficult to put on in such a way that it will be comfortable here.

Several years ago in Baltimore, I talked with Dr. Griswold about the hanging cast and saw his exhibit, and I was sold on the idea that this was the thing for me to use. I felt that my worries were over and if anybody came in with a broken humerus after that all I would have to do would be to put on one of those things.

I found out later it was not so good as that. However, I have used it and, much to my surprise, the results were good. I could not see why, anatomically or theoretically, at first. I have used it in very thin individuals weighing probably a hundred pounds and also on one negro woman weighing over two hundred pounds, as well as type ranges between these extremes.

Enough emphasis has not been placed upon securing 100 per cent cooperation of the patients, or nearly that. They can sling the arm around to the point that what little callus might try to form would be disturbed every day or two, and we have then a long, drawn-out period of treatment.

I had such a case recently. It was impossible to get any sort of cooperation from the patient, and I thought the arm would never heal, but I did not abandon the hanging cast and got good union at the end of about fourteen weeks.

I have made the cast a little bit lighter than I thought was needed, and later added a little plaster around the elbow or below it to give additional traction as necessary.

I believe the hanging cast has merit, and I am going to continue to use it until some of you gentlemen present something better.

Dr. Eve (closing).—I agree with everything Dr. Conwell said in regard to the treatment of fractures of the shaft of the humerus. Eight or ten years ago we placed the arm in too much abduction, usually from 70 to 90 degrees, but now we place it in only from 15 to 30 degrees.

I notice Dr. Key is using the hanging cast method with good results. However, I believe with this method, with a complete fracture and with typical symptoms, the patient should be in a hospital for the first few days.

I agree with Dr. Carruthers, that fractures of the shaft of the humerus do not require much traction. Reduction of the fracture is usually not difficult.

I still like the Gurd method, or the slight abduction method of plaster cast. However, in selected cases, I am now using the hanging cast method. I agree with Dr. Netto that if you have a cooperative patient and selected cases, the hanging cast is the method of choice.

THE IMPORTANCE OF PRIMARY CARE IN THE TREATMENT OF COMPOUND FRACTURES*

By H. WINNETT ORR, M.D.
Lincoln, Nebraska

For many years now I have been asking physicians and surgeons what they think about their results in the treatment of fractures. With few exceptions, they think their results are good. Statistics, however, do not bear them out in this opinion. Figures gathered from many sources show that, in simple fractures, deformity and disability are to be found in from 5 to 10 per cent of all cases. In compound fractures the results are much worse. Not only is disability severe and prolonged, but there are amputations, deformity and permanent incapacity for work in nearly 50 per cent of all cases. In compound fractures of the leg and femur there is a certain death rate; and the percentage of permanent disability in certain large series of cases has been as high as 70 or 80.

I am a little disturbed to find the attitude toward these cases in your meeting yesterday, that the problem in compound fractures is a wound problem. One of the speakers scarcely mentioned the fracture and another said anyone

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could treat a fracture if the wound were left open. I think it is better to say that anyone can treat a wound if the wound is left open, but *the fracture must have correct fracture treatment.*

I shall begin by saying that these poor results are due in part to the fact that there has been as much tinkering with the principles of fracture treatment as there has been with the splints and apparatus which are an essential part of fracture care. We all agree that the first requirements for the care of a fracture are reduction of the fracture and maintenance in correct position until healing has occurred. But even the textbooks tell us that these principles must be applied, not strictly, but with a due regard for the character of the injury, for the circumstances surrounding the patient, for the experience of the attending surgeon, and for the kind and amount of hemorrhage, shock and wound infection found at the time the patient presents himself for treatment.

What we should say instead is that, regardless of circumstances, every fracture should be reduced immediately. It may be assumed that every surgeon will deal with emergency or late complications as efficiently as he can. But he must either be able to "set the fracture" himself, or he must secure competent assistance in doing so. The bone fragments should be placed in correct position and the surrounding anatomical parts should be arranged in proper anatomical relationship to each other. Then the injured limb should be immobilized in a kind of apparatus in which improper motion, muscle spasm and pain are impossible, and the patient should be guarded in that position. Finally, the infrequent dressing method in a plaster-of-paris cast enables us to subordinate the care of the wound to the treatment of the fracture in all cases.

For the prevention of gas gangrene it is only necessary to have an open wound with good drainage and access of air to all parts of the wound. The petrolatum pack and the cast constitute such a dressing. The moment you close any part of any contaminated wound with stitches or even insert rubber tubes, you provide closed pockets in which tetanus, gas bacillus and other infections may develop. We do not have these complications.

One of our difficulties in fracture treatment is that too many fractures are treated by physicians and surgeons of limited training and experience. Some years ago I studied a series of 1,300 fracture patients in a small city. These were practically all the patients in five hospitals over a five-year period. Of the 1,300 patients, about 60 per cent were treated by four surgeons with special training and experience in dealing with fractures. Eighty-nine other surgeons and physicians treated the remainder of these fracture patients. Thus, about 40 per cent (or over 500 patients) were treated by surgeons and physicians who treated in some cases only one fracture during the entire period, and the largest number treated by any other physician or surgeon of the 89 was eight. I shall spare you my analysis of the results in the 40 per cent, but can say that loss of time and permanent disability were much higher in those treated by physicians and surgeons with a limited experience in such cases.

In 1918, during a rather extensive military experience, I became dissatisfied with the Carrel-Dakin method. The continuous irrigations and the frequent changes of wet dressings caused too much movement of the injured parts, too much muscle spasm, and too much pain for patients with compound fractures of the extremities. Also, I observed that wounds frequently exposed were often contaminated so that even the irrigation with Dakin fluid was insufficient to prevent or control the inflammatory complications that supervened.

A practice that became common was to pack the wound with a wet Dakin dressing and leave it for twenty-four hours. After I proposed my method some surgeons put in Dakin packs and left them for several days, or even longer. It was absurd to attribute good results which followed such treatment to the Dakin solution because Carrel and others had shown that the solution remained active chemically in the wound for only a matter of minutes rather than hours or days.

Even in 1918, influenced by the teaching of Dr. John Ridlon and Sir Robert Jones, I began to advocate better fracture reduction, better control of the fragments, better immobilization of the limb, and less disturbance of the wound. By 1923 I had described a plan of treatment which has since become known as the Orr method. This calls for prolonged immobilization by fixed traction. All the parts are maintained in correct position, and there is prolonged protection of the wounds against complications due to secondary and mixed infection. This method represents a combination of the teachings of Sir Joseph Lister and Hugh Owen Thomas. Lister's original proposal was for the "antiseptic" pro-

tection of wounds against the invasion of micro-organisms by "exclusion." Hugh Owen Thomas throughout his entire life taught the importance of immobilization for all infected and inflamed parts "enforced, uninterrupted and prolonged" as the most important contribution a surgeon could make to his patient's recovery.

In his later years Lister was persuaded by his pupils and his associates to depart from his original plan of excluding infection and to engage in the search for a chemical cure. That search is still in progress, and I shall have more to say about the present status of the search before I finish this paper.

Fundamental requirements of fracture treatment are often modified or neglected for the reason that their full import is misunderstood. It is not sufficient merely to place fracture fragments in a broken limb end to end and to apply a splint in that position. Every surgeon who reduces a fracture should have in mind the importance of readjusting into correct anatomical relationship all the parts of the limb in which a fracture has occurred. The restoration of physiologic function to an injured limb requires not only the readjustment of the bones, but the replacement of all the nerves, vessels, muscles and tendons in such a damaged extremity. The setting of the bones and the limb having been accomplished, immobilization in correct position then becomes the only necessary further contribution to the patient's recovery.

Disregard of these requirements of reduction and control is often justified upon the ground that the wound requires treatment. During the past twenty years we have demonstrated conclusively that frequent dressing of wounds is unnecessary. It can be stated simply and positively that if drainage and protection are provided, if the wound is left open, filled with a pack which maintains drainage, and then protected under the cast against secondary trauma or infection, the patient will recover.

One speaker said yesterday, dogmatically, that sulfanilamide packed into a wound diffuses at once and continuously into the surrounding tissues. Upon the study of laboratory workers in whom I have confidence, I should say that through the surface of an untraumatized, granulating, healing wound surface there is no diffusion of chemicals or germs at all. If a wound surface is damaged daily or frequently, some materials and organisms can be forced through it—but always to the patient's harm. It has always been my opinion that what is done or what happens between the wound surface and the wound dressing makes very little difference to the healing of the wound or the fracture. If the wound surface is not damaged, if there is adequate drainage and *if the fractured limb and the patient* are really at rest, then we have all the injured parts in correct position for circulation, nerve supply and immediate and ultimate best function. But I do not agree with Dr. Key, who said yesterday that anyone can treat such a fracture case successfully if only the wound is left open.

Since I first described my method in 1923, there have been many modifications and alternatives proposed. I shall refer briefly to only three of these.

First, the viable antiseptic or maggot method of Baer. This method followed my suggestions in a general way as to less frequent dressings and the treatment of the limb in plaster-of-paris casts. Baer proposed maggots, however, as a substitute for my vaselin pack. He said the maggots would clean up the wound and in some way "promote healing," but Baer's method has never given better results than former frequent-dressing methods. Baer's suggestion that the maggots supply some kind of a "healing principle" has not been confirmed. In my opinion, Baer's[1] contribution to the Post Graduate Assembly in Detroit in 1929 and to the Congressional Committee in Washington on April 17, 1930, are two of the most peculiar documents in medical literature. The method, while widely discussed at the time, has now been abandoned. That the maggot method should have gained even temporary acceptance is difficult for me to understand.

A second suggestion was by Dr. Fred Albee, of New York, who proposed that my results (which he had confirmed in his own practice) were due to bacteriophage. Albee prepared bacteriophage in his laboratory and added that to the dressings in those cases in which it could not be found. But no clinical evidence has as yet been adduced to show that with bacteriophage added, patients do any better than those without. I have never used bacteriophage as a therapeutic agent and except in a few special cases have not known whether or not it was present in my patients' wounds. But my statistics now for several thousand cases of compound fracture treated in my own practice and in cases reported by others, have shown cures in 85 to 90 per cent,

1. Baer: Proceedings of the International Post Graduate Assembly, 5:365-372, 1930.

which is far higher than any reported by those who employ irrigation or antiseptic dressings.

In the third place, we must consider those methods of chemotherapy which have been modernized to the extent that chemicals are now employed intravenously for the cure of wound infection.

You will all remember the excitement aroused by the claim from the Johns Hopkins Hospital about ten years ago that the long-sought-for ideal antiseptic had been found in mercurochrome. Now it is sulfanilamide. If you will compare the literature of the two chemicals you will find that the statistical tables, the clinical claims and the variations in technic promulgated for sulfanilamide at the present time are almost repetitions of the mercurochrome literature of a few years ago—but no one uses mercurochrome at the present time.

It does appear to have been demonstrated that sulfanilamide and some of its modifications and derivatives have a selective action on the type III pneumonia organism, upon the meningococcus, and upon the gonococcus, perhaps also upon certain strains of the streptococcus. That it is possible to induce a degree of antisepsis in the blood stream for even these organisms, however, without damage to the patient has certainly not been demonstrated. It is admitted also, even by enthusiasts for intravenous sulfanilamide therapy, that for the staphylococcus even this chemical is not efficient. Moreover, it is not yet known whether sulfanilamide does act as a bactericide or whether the apparently germicidal action in some cases is due to an antiseptic response on the part of the patient.

Most compound fracture infections that cause prolonged osteomyelitis and disability are caused by the staphylococcus. It is important to observe, therefore, that by the plan of treatment I have proposed a high per cent of patients have recovered without those complications which are commonly supposed to call for chemotherapy. When chemotherapy is employed along with my method, allowance must be made for the fact that the patients may be recovering, not because of the chemotherapy, but because of the other treatment. As indicated above, my program has already proven effective in a high percentage of all cases without the use of chemicals at all. Patients may as well be spared the dangers of sulfanilamide poisoning if the treatment is adequate otherwise.

Alarm over certain blood conditions in these patients and satisfaction over apparent improvement following chemotherapy are not yet fully understood. Undoubtedly these changes, although unknown to us, have always been occurring in patients getting worse and getting better.

A final suggestion which has become a topic for discussion recently is that of filling the wounds with sulfanilamide. (Twenty years ago it was Dakin's solution.) Fractures are reduced, casts put on and the patient is then left without subsequent dressings as I have proposed. I have stated on many occasions that the exact form of dressing put on at the time of primary treatment or operation is unimportant. If we fill the wound with sulfanilamide and the rest of the program is the program I have described, I cannot join with those who attribute the ultimate result to the chemical employed. Filling the wound with sulfanilamide or any other chemical is only to put in the wound a substance which becomes inefficient in a few hours or in a few days and the patient himself must be credited with the recovery that takes place from then on. Even with a sulfanilamide dressing for a day or two it is my method for the remainder of the month or six weeks that the dressing and the cast are left alone. With the recovery of the patient, or even with the healing of the wound, the pack has little to do except to provide the very important primary drainage.

There are several distinctions that are important to make in discussing the treatment of compound fractures. These have to do with what is meant by early treatment, primary treatment, postoperative care and secondary treatment. I have felt that the treatment instituted at the time of injury should be spoken of as early treatment rather than primary treatment. Early correct treatment is the most important kind of treatment to secure for a compound fracture patient. Early treatment should be made up of: First, traction and manipulation reduce the fracture. Second, debridement and provision for drainage of the soiled or infected wound. Third, fixation of all the parts so that there is perfect control without constriction or pressure. And fourth, after-care as necessary to maintain such control and to protect the wound against secondary infection until healing takes place. That is a correct description of early treatment and postoperative care. Primary or even secondary closure of soiled or infected wounds should be done rarely, if ever. Occasionally successful operations of this sort by no means justify their general employment.

Primary treatment is the treatment required

for any severe compound fracture, no matter at what stage, in which correct treatment has not yet been instituted. It is for this situation and for this patient that I have chosen the title for this paper, and for which and for whom I make a special plea. When you or I are called in consultation for a compound fracture patient, certain difficulties or complications have become so serious that the time for correct primary care has arrived. Such primary treatment must consist of traction and reduction of the fracture, even if a surgical procedure is necessary. This may mean traction, manipulation, surgical operation, direct fixation of fragments, provision of drainage, the insertion of skeletal pins and the application of a splint or cast. Such a program is truly primary treatment with provision for correct postoperative care.

Secondary treatment is late treatment for a patient for whom a good result has not been obtained. Such secondary care usually means operation, correction of shortening or deformity, sometimes osteosynthesis, drainage for chronic osteomyelitis, or/and a complete course for the treatment of the fracture as described above.

In all of these, especially in the presence of infection, traction, manipulation and reduction of the fracture, drainage of the wound, protection against postoperative infection, and immobilization in correct position are the fundamental and essential parts of the treatment program.

Dr. Baker remarked yesterday that early drainage is necessary if we are to get best results in staphylococcus antitoxic and sulfanilamide therapy. I think that sentence should read: Early drainage is necessary if any osteomyelitis or compound fracture patient is to have his best chance for recovery at all!

It is just as important to protect a wound or a sinus that is draining pus as at any earlier stage. Many wound and fracture complications of the most serious character occur late because of accidental mixed infections. Dressings, drainage tubes and even wound inspections subject the patient to this danger. Finally, any surgeon who finds himself in doubt as to his ability to comply with all the requirements of this program should associate with him, at the very beginning of the care of a compound fracture patient, such consultation or assistance as may be necessary.

DISCUSSION (*Abstract*)

Dr. Duncan Eve, Nashville, Tenn.—How do you deal with acute fractures, compounded, where tendons and muscle are involved?

Dr. Orr (closing).—I think I can give you no better answer than to say that we do as nearly like Sumner Koch, of Chicago, and some of the other men who do fine tendon and nerve work in hands and feet, as we can. We do a primary clean-up procedure, a debridement, if you want to call it that, including thorough scrubbing with soap and water when necessary and repair immediately all tendons and nerves that we can repair without taking too much time. That depends partly upon the condition of the patient.

We fix up these patients soon after injury with immediate traction and immobilization. We have not the same apprehension about shock as with ordinary methods. These patients do not have shock. If we get the arm or leg in full length, and the muscles and other structures restored to as nearly anatomical arrangement as possible, the patients do not have shock, and it is possible to take more time to do things. Of course we give fluids and such medication as may be indicated.

But we do attempt to repair, as far as we can, and without doing further damage, all the tendons and muscles and nerves that are badly torn.

Question.—Do you leave them open?

Dr. Orr.—I never use a needle and thread to close such wounds or use rubber tubes for drainage. The petrolatum pad or pack affords drainage for all secretions and permits access of air which is the best prophylaxis against anaerobic complications.

A COMPARATIVE STUDY OF THE TREATMENT OF COMPOUND FRACTURES*

By RUTH JACKSON, M.D.
Dallas, Texas

Progress of men, of nations and of science is born of discontent. In 1877, the mortality rate in patients with compound fractures was estimated as 40 per cent. Lister then introduced his antiseptic dressings and the death rate, as well as the incidence of infection, dropped markedly. Further reduction in fatalities and infections was noted when Volkmann and Bramann, in 1901, and Trendelenburg, in 1906, practiced the conversion of compound fractures into closed fractures by primary excision and suture of the wounds. During the first World War the Carrel-Dakin method and the Orr method of treating open fractures were used with still better results. Very little progress was noted from that time until 1933, at which time Kelly[1] reported a small series of compound fractures infected with gas bacillus organisms which he had successfully treated with x-radiation. He has reported further studies[2] in prophylactic x-radia-

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

tion as well as in therapeutic x-radiation. It is not known whether the action of the roentgen ray is physical, biological or chemical, but certainly no one can question its value.

Since 1937, sulfanilamide in all its forms and dosages has been given by mouth to patients with potentially infected and infected compound fractures. Variable results have been reported, but on the whole they have been encouraging. Sulfanilamide and x-radiation have been used concurrently; however, the results have been less satisfactory than when they were used separately. Kelly[3] has said that there are definite contraindications to the use of the two at the same time and that the x-ray effect in inflammations is definitely inhibited by the simultaneous administration of the sulfanilamide group. The *in vivo* experimental work of Fluks *et al.*[4] was consistent with Kelly's contentions, and they concluded that there was no synergistic reaction demonstrable between sulfanilamide and roentgen rays.

In July, 1939, Jensen, Johnsrund and Nelson[5] reported forty-one cases of compound fractures and dislocations which had been treated by debridement, local implantation of sulfanilamide crystals, and primary closure. No primary infections occurred. Key and Burford,[6] in November of 1939, reported their experimental work on the effect of sulfanilamide in the healing of compound fractures. They concluded that the local implantation of sulfanilamide in compound fractures not only lessened the danger of infections, but that it did not interfere with the healing of the soft tissues or of the bones. Marshall[7] has said that sulfanilamide affects the invading organisms as a result of bacteriostatic and bacteriocidal action, which in many cases is not sufficient to effect sterilization without the cooperation of the defensive reaction of the host. This probably accounts for the occasional infection that occurs.

On the author's fracture service at Parkland Hospital we began in 1936 using x-ray therapy in the treatment of compound fractures with gas bacillus infections. The results in a few cases were excellent. In 1937, we instituted routine prophylactic x-radiation of all compound fractures and noted not only a drop to nil in gas bacillus infections, but fewer pyogenic infections. Then with the hope of further reducing pyogenic infections, a series of cases was given prophylactic x-radiation and oral sulfanilamide, but with somewhat discouraging results. Since December of 1939 we have used sulfanilamide crystals or powder locally in most of the compound fractures and have closed all wounds by primary suture.

A comparison of the results of these methods of treating open fractures has proven interesting and well worth consideration. All cases in these series received thorough debridement according to the accepted standards, no antiseptics were used in the wounds, and all wounds were irrigated with copious amounts of normal saline solution. Mixed antitetanic and perfringens serum was given to all cases as a prophylactic measure.

Of fifty cases treated by debridement, twenty-seven, or 54 per cent, became infected with pyogenic organisms; five cases, or 10 per cent, developed gas bacillus infections, two of which were treated by x-ray with recovery, two patients died, and one recovered after amputation; five, or 10 per cent, came to secondary amputation; and three patients died. No internal fixation was used. The average hospital stay was thirty-seven and seven-tenths days.

Of fifty-seven cases treated with debridement and prophylactic x-radiation of 100 r units on three successive days, nine, or 15.8 per cent, developed pyogenic infections; no gas bacillus infections developed; no secondary amputations resulted; and no deaths occurred. No internal fixation was used. The average hospital stay was 19.8 days.

Of sixteen cases treated with debridement, prophylactic x-radiation and oral sulfanilamide, seven cases, or 43.7 per cent, became infected with pyogenic organisms; one case developed gas bacillus infection; no secondary amputations resulted; and one case died. No internal fixation was used. The average hospital stay was twenty-two days.

Of fifty-four cases treated by debridement and local implantation of sulfanilamide crystals or powder, three cases, or 5.6 per cent, developed pyogenic infections; no gas bacillus infections occurred; no secondary amputations resulted; and no deaths occurred. Internal fixation was used in eleven cases. The average hospital stay was 6.8 days.

Case 15 (*Table 1*) of the latter series became infected with *Staphylococcus albus* organisms probably because of a lack of the proper defensive reaction of the patient. She was a degraded prostitute and a narcotic addict.

Case 35 (*Table 1*) of the same series had multiple compound fractures of both legs, feet, and the left hand caused by a cave-in of a gravel

Table 1

Type of Treatment	No. Cases	Pyogenic Infections		Gas Bacillus Infections		Secondary Amputations		No. Deaths	No. Cases in Which Internal Fixation Was Used	Average Hospital Stay, Days
		No.	Per Ct.	No.	Per Ct.	No.	Per Ct.			
(1) Debridement	50	27	54	5	10 Two treated with x-ray and recovered; two died; one amputation with recovery	5	10	3	0	37.7
(2) Debridement and prophylactic x-radiation	57	9	15.8	0		0		0	0	19.8
(3) Debridement, prophylactic x-radiation and oral sulfanilamide	16	7	43.7	1	6.3	0		1	0	22
(4) Debridement and local implantation of sulfanilamide.	54	3	5.6	0		0		0	11	6.8

pit. All the wounds were filled with gravel, and there was severe pressure necrosis of the entire left leg. Doubtless this leg should have been amputated in that the tissues of the entire medial side of the leg sloughed, and this wound became infected with *Staphylococcus albus* organisms. The other wounds, however, escaped infection.

Case 36 (*Table 1*) received multiple severe compound fractures of the right hand when the patient fell under a train. He traveled many miles to get to Dallas for treatment, and some eleven hours had elapsed before any treatment was given. It was necessary to amputate the hand at the wrist joint. Some seven days later a mild *Staphylococcus albus* infection developed in the superficial tissues of the stump, but cleared up promptly with no ill effects. This patient was also a derelict and a narcotic addict.

From this comparative analysis we can conclude that prophylactic x-radiation of compound fractures lessened the incidence of pyogenic infections and gas bacillus infections, shortened the average hospital stay, and reduced the number of secondary amputations and deaths to nil. It has shown, also, that the results in cases receiving both x-radiation and oral sulfanilamide were less satisfactory. Lastly, it has shown that local implantation of sulfanilamide crystals or powder in compound fractures after thorough debridement is by far the treatment of choice. It has removed the fear of using internal fixation in these fractures which from an economic standpoint, as well as from the standpoint of ultimate functional and anatomical results, marks the greatest progress in the history of the treatment of compound fractures.

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DISCUSSION (*Abstract*)

Dr. Brandon Carrell, Dallas, Tex.—To my knowledge, this is the largest reported series of compound fractures in which sulfanilamide has been used locally, and since Dr. Jackson actually did, or supervised the majority of the cases reported, the group comparison also has greater significance.

It would almost lead one to believe that sulfanilamide is a magic powder which banishes the fear of infetion, but since its action is primarily bacteriostatic, it should be emphasized that the chief principles in the treatment of compound fracture are still adequate careful debridement and proper fixation. From the results

in this series it is apparent that these principles have been faithfully adhered to.

Although our series is not impressive, in those cases in which we have used sulfanilamide locally the results have been quite pleasing, and I believe typical of those of others who have used it. The fear of using internal fixation, which is frequently of great advantage, has been materially diminished.

It has also given some feeling of security in reopening for the purpose of secondary fixation or bone graft, older compound fractures which have only recently stopped draining. We have not, however, felt sufficiently safe in the primary closure of all cases, and in some, especially those of over twelve hours' duration, have covered and debrided surfaces with sulfanilamide crystals, packed with vaseline gauze and applied plasters which are not windowed for dressings. We feel that this method is more gratifying than the use of plain vaseline or scarlet red gauze alone, but we have not yet used non-padded plasters as advocated by war surgeons in Spain.

We are at the present time carrying out some animal experimentation on the efficiency of sulfanilamide in preventing gas infection, but the results are not yet ready to be reported.

The local implantation of sulfanilamide is a great step forward in the treatment of compound fractures.

Dr. Harold R. Bohlman, Baltimore, Md.—In December of 1936, I treated the first infected traumatic wound of a hand with sulfanilamide, with immediate success. In January, 1937, I treated the first gas gangrene case, a hopeless one, by a long, deep incision and the administration of sulfanilamide by mouth, with rapid recovery from the gas gangrene, but with a secondary osteomyelitis which subsequently cleared up. Following this I treated two more gas gangrene cases. The three were reported in the *Journal of the American Medical Association* of July, 1937, and at that time I suggested the prophylactic use of sulfanilamide in the treatment of compound fractures and traumatic wounds, for I had already used it locally and systematically in this manner. Following this publication, the use of sulfanilamide in traumatic wounds and compound fractures spread rapidly around the world.

At the present time, we have a back-log of some two hundred and twenty cases, of which forty-four are gas gangrene cases from various sources and workers, with a mortality of 8.7 per cent. Many of these were in bad shape before sulfanilamide was administered.

Out of the two hundred and twenty cases, one hundred and forty-eight are compound fractures recorded in the Johns Hopkins Hospital. Sixty of these were treated with sulfanilamide, forty-eight of the sixty prophylactically, twelve curatively for gas gangrene. In these there were two deaths, or 3.3 per cent mortality, with sulfanilamide given by mouth. Incidentally, these two deaths occurred in operative wounds, one a brain and another an abdominal operation.

In Johns Hopkins Hospital in the last three years we have had no deaths from gas gangrene in a traumatic wound or a compound fracture, since we have employed sulfanilamide in those cases. Compare this mortality with Kelly's, which is about 10 per cent, or 40 to 70 per cent in the literature before the advent of x-rays or sulfanilamide therapy.

A word about circulation. It is absolutely essential to maintain arterial, venous and capillary circulation in treating traumatic wounds or compound fractures. If circulation is not maintained, sulfanilamide in sufficient concentration cannot reach the affected part, and bacteria or gas bacilli will multiply far beyond any cellular response in the tissues. We have sections showing this. If gas gangrene or gas infection occurs, gas itself acts as an internal pneumatic tourniquet, obliterating circulation further.

I believe that a thorough wound toilet should be done, as Dr. Jackson said, but with little if any debridement. I have treated ten cases in which no sterilizing solution or substance or material whatever was used, either in the wound or on it. A thorough lavage with normal saline was done and the wound packed or merely covered with vaseline gauze, a plaster splint applied and sulfanilamide administered by mouth until we had ten milligrams per cent. Some of these cases had no washing whatever, simply a vaseline covering, a splint, sulfanilamide by mouth, recovered with healing per primam, without infection or signs of it. In others we cultured staphylococci from the secretions in the wounds, but they healed readily.

Just a word about the Orr method or Trueta's method. There seems to be an impression that the latter has originated a new method or treatment. Trueta worked in Barcelona in the Spanish Civil War. He is a true disciple of Winnett Orr, and reports five thousand cases in which he used plaster splinting with vaseline gauze packs after debridement. Some half million of his countrymen were refugees in France and ten thousand of these were wounded. The French surgeons did what they called "amputations of urgency." Some of these people appeared walking with compound fractures in these plaster splints, some wounds recent and some old, some smelled to high heaven. This scared the French surgeons badly, and they began taking off limbs promiscuously. Apparently tiring of this, they stopped, and found the patients recovering without trouble. Arnaud reported a series of eight hundred of these to the Academy of Surgery in Paris.

Regarding the closure of compound wounds, I feel that it is inviting trouble. Lenhard, a colleague in Baltimore, head of a very active fracture service, in thirteen years has not seen a single case of gas infection, and in thirteen years he has not closed a single compound fracture!

Implantation of sulfanilamide is of great value. One can raise the concentration to about eight hundred milligrams per cent locally, and at that level it is hard for any bacteria to grow or even exist. It does, however, have the disadvantage of producing a violent chemical reaction, and with closure of the wound one may look for trouble with circulation. I have seen ischemic paralysis result from this manner of treatment. I now have used local implantation in about one hundred cases, so that my experience is fairly large. It does slow healing of soft tissues and of bone. Dr. Key has remarked to the contrary, I believe, in a recent article,

but I believe absorption was sufficient to affect healing of the control side.

Incisions should be made through skin and fascial planes to release tension and should be longitudinal in the extremities.

Gas antitoxin I feel has little value. Time and again I have seen gas gangrene develop when it has been given prophylactically and now I no longer use it. The ten cases treated without sterilizing solutions in the wounds received no gas antitoxin, only tetanus antitoxin.

I have seen three or four gas gangrene cases develop where x-ray therapy had been used prophylactically. We have not employed this technic in Johns Hopkins. I have seen cases moved from the bed to the stretcher, from the stretcher to the x-ray table, then back to the stretcher and to the bed, with huge compound fractures in which I am sure the shock and the trauma of movement did far more damage than the x-rays did good. X-ray therapy has the disadvantage of requiring a cumbersome apparatus, and in the field in war it is not readily applicable, while sulfanilamide can be carried by a soldier, and he can be instructed to use it if he is conscious. X-ray does not relieve tension. One must remember surgical principles. We have had some severe reactions where sulfanilamide and x-ray therapy were combined. Its effect seems to be momentary mutation of the bacteria in growth.

Cohen and Sculenburg, writing in the *Lancet* on the British Expeditionary Forces evacuated from Dunkirk last summer, cite two hundred and sixty-six cases of gunshot wounds with no gas gangrene, with one amputation, with no deaths. These cases were treated by the Orr-Trueta method and were given sulfanilamide by mouth. I have written the surgeons-general all over the world regarding the use of sulfanilamide, and I have a memorandum issued by the British Surgeon-General to his officers on the dosage, which is immediate and sufficient for effective concentration in the blood. The combined Orr-Trueta method with sulfanilamide made the above record under war conditions. Ten primary closures in this group all became infected. Incidentally, some of them formed staphylococcal pus pools which were sterilized by the use of sulfathiazole.

Colonel Kirk, in our Army, has advised the use of sulfanilamide either in powder form in the wound or by mouth, or both, and I believe our soldiers are going to carry it.

To sum up, we must pay attention to circulation. We must lavage wounds. I believe we should avoid debridement. I have seen more damage done by the surgeon's scalpel than the original trauma, far more in some cases than occurred with the trauma.

I believe the Orr-Trueta method is preferable to wound closure, and I firmly believe in the prophylactic use of sulfanilamide locally and systemically.

Dr. J. Albert Key, St. Louis, Mo.—It was my impression that in Baltimore sulfanilamide was not used locally, but by mouth. I am glad that they are learning to use it locally, because I have emphasized that by mouth it is relatively ineffective.

I think that Dr. Jackson's series of fifty-seven cases is the largest that has yet been published. I want to emphasize the fact that a thorough debridement is absolutely necessary; not only that, but it is extremely important to get all foreign material out of the wound.

Sulfanilamide does not kill bacteria; it inhibits their growth. If you leave foreign material in the wound that is infected, if you leave necrotic tissue in the wound that may harbor infection, bacteria may remain two or three days until the sulfanilamide has gone, and then the wound starts to suppurate. That does happen; I have seen it happen.

Sulfanilamide is not a magic powder, and nothing that was done before can be omitted. You have to do just as good surgery as ever. The only difference is that you are going to get better results if you use sulfanilamide locally. I do not think that the use of sulfanilamide by mouth will make very much difference in the incidence of infection.

As far as leaving the wounds open is concerned, anybody can treat compound fractures if he leaves them open. That is no advantage. But Dr. Jackson has closed 100 per cent of hers and had only three infections in the fifty-seven. She has cut her hospital stay down to six and a fraction days, and she did that because she closed her wounds.

Dr. F. Walter Carruthers, Little Rock, Ark.—I reported a series of seventy-five cases recently in which 75 per cent of the cases were compounded. I did not have a single infection in any of those, and they were all treated as Dr. Jackson has treated hers. I most heartily agree with her.

Dr. Jackson (closing).—To Dr. Bohlman I offer my apologies for not knowing about the cases he reported prior to the ones I mentioned.

As far as debridement is concerned, I think it is most important to cut away all macerated or dead tissue because such tissue, if not removed, makes a very good spot in which organisms grow. I remember a child in my series of cases who had a simple puncture wound in the leg from a fracture of the tibia. My first inclination was to clean up only the edges of the wound and fill it with sulfanilamide. However, I decided it would be better to open the wound and do a thorough debridement. I enlarged the wound longitudinally and there was, in spite of the fact that you could not tell it from the outside, a tremendous amount of damage done to the soft tissues. This wound in all probability would have become infected if it had not received a thorough debridement. I feel definitely, therefore, that in all cases which are to be closed primarily a thorough debridement of the wound should be done.

X-ray therapy does not require moving the patient from the bed, as it can be given with a portable x-ray machine. We do not, of course, use it now in wounds that have been treated with sulfanilamide.

Only five and six-tenths per cent infections in fifty-four cases treated by local implantation of sulfanilamide and primary closure convinces me that this is the treatment of choice, and when sulfanilamide is used locally one need have very little fear of closing the wounds by primary suture.

THE ROLE OF DEEP X-RAY THERAPY IN PRURITUS VULVAE*

By WILLIAM E. EASTLAND, M.D.
Oklahoma City, Oklahoma

Much has been written on the subject of pruritus vulvae, but the literature on deep x-ray therapy of the condition reveals that foreign writers have contributed a comparatively few essays, and in our country there has been much less. It is because of the scarcity of work on this method of treatment that it has been selected for a brief report today.

The etiology of pruritus vulvae is decidedly unsettled, according to the various authors who have written on the subject. Pusey[1] believed that pruritus vulvae might be a sequence to pruritus ani; moreover, that the latter was due to residues from feces causing skin irritation and in turn itching.

Buie[2] questioned the belief that anal pruritus is due to fistulas, fissures, ulcers of the anus or rectum, or benign and malignant polyps, or hypertrophy of papillae and varicosities. On the contrary, Montague[3] observes that the majority of cases of anal pruritus is due to colproctitis, fissures, fistulas and hemorrhoids. O'Donovan[4] has found in 83 cases of pruritus ani et vulvae no discoverable cause. MacKee[5] treated 210 cases of pruritus, most of which involved the vulva and anus, without detecting the cause. Hailey and Hailey[6] reviewed 139 cases, finding that 80 per cent had patches of eczema on other parts of the body as well as on the vulva, and 60 per cent of their series revealed one or more forms of allergy in one or more immediate blood relatives. Hence, they believe that the condition is essentially eczematous.

Exemplary of one cause of pruritus vulvae is a case that I recently examined with a history of pruritic symptoms for several months. After hysterectomy for a fibroid uterus, all itching ceased. The patient had been totally unaware of her fibroids.

Among the chief considerations otherwise thought to be related to pruritus vulvae, as cited by Burnam,[7] are dermatitis due to infection or chemical irritation, parasitic infection, gonorrhea of Skene's duct, Bartholin's glands, the urethra and the epidermis, leukoplakia and kraurosis vulvae, vaginal discharges from vaginal and uterine pathology such as Trichomonas, yeast and Monilia in the vagina. Pruritus vulvae of neurogenic origin is a definite and important type. Hormonal and other deficiencies have a distinct place in the etiology.

Although the title of this essay alludes to the role of deep x-ray therapy in pruritus vulvae, it would be amiss not to mention the use of superficial x-ray therapy as well as other agents. By employing such x-rays in treating common skin diseases which also involve the vulva, causing pruritus, it is ordinarily possible to obtain as good results here as in lesions situated elsewhere on the skin. Therefore, it seems better to employ superficial x-rays for such conditions as dermatophytosis, eczema, intertrigo, folliculitis, furunculosis, seborrheic dermatitis, and so on, of the vulva. Under such conditions the response from low voltage x-rays seems sufficient as the pathology apparently is superficial enough to be favorably influenced without resorting to the more penetrating effects of high voltage x-rays. The technic of superficial x-radiation is too well established to discuss.

Aside from physical agents, there are other measures in the treatment of this condition that sometimes alone may serve to effect a cure or, if used with x-rays, they act as important adjuncts. Angus[8] says that there are two essential points: first, all scratching must be forbidden; second, contamination of the irritated part must be prevented by application of vaseline or oil before defecation or urination, careful cleansing afterwards, and keeping the parts dry. Of course, such care is particularly necessary in those cases in which there is a related vulval and anal pruritus.

It is not within the scope of this article to delineate the various topical applications that are important in relieving pruritic symptoms and overcoming cutaneous changes produced by scratching, and also lesions characteristic of skin diseases. Moreover, it is not the intent to describe medical management or other procedures in various affections arising in the vagina or pelvic organs that cause pruritus vulvae.

Attention is now drawn to the value of deep x-rays in pruritus vulvae. Some seven or eight years ago I occasionally gave one or more exposures of deep x-rays to this affection. Within the last three or four years I have administered it more frequently and have been under the impression that its results are superior to super-

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ficial x-rays. This applies particularly to those cases in which the objective symptoms, if any, have been produced by traumatic scratching resulting in fissures, excoriations and finally lichenification. To some of these cases various writers have assigned a neurogenic origin, while others are simply classed as essential or idiopathic. Although the exact cause is unknown, it is in these cases that ordinary measures have failed to give satisfactory results.

It is apparent from the literature that more European workers have used high voltage x-rays in pruritus vulvae than in the United States.

The technic of deep x-ray therapy for pruritus vulvae, as with other conditions, is somewhat variable, depending on the radiologist. Delhem and Fauseller[9] administer 60 to 120 r every other day for a total of 800 r. Also, they radiate the back to affect the roots of the lower lumbar and sacral nerves. Wobker and Rauft[9] employ a technic of 6 ma., 200 kv., 70 cm. distance, 0.5 mm. copper, producing 640 r per treatment, which is 80 per cent of a skin erythema dose. It is repeated in two weeks and again in six weeks, if necessary.

Kolde[10] considers that x-rays affect the nerve terminals or the innervation of the vascular supply. It seems quite possible that not alone are the nerve endings influenced by x-rays, but also nerve roots and their ganglia, as is evidenced by the findings of improved results in the cases of Delhem and Fauseller, who radiate the nerve roots of the lower lumbar and sacral nerves.

Highly satisfactory results, of course, are not common to any form of therapy in pruritus vulvae. Wobker and Rauft compiled their results as follows:

	Cases	Cured	Improved	No Change
After climacteric	19	5	9	5
Before climacteric	11	3	6	2

These cases were treated with 200 kv. x-rays.

Schafer's[11] results with deep x-rays and grenz rays are:

Cases	Cured	Greatly Improved
37	12	5
26	8	

Burnam reports twenty-two cases treated by 200 kv. x-rays with twelve failures, five of which had no gross lesions, seven with advanced kraurosis and leukoplakia. Ten of the twenty-two cases had complete relief for two to fifteen years.

Kolde treated fifty-eight cases by deep x-rays, obtaining thirty-nine cures. Thirteen were improved, three not improved and four could not be traced. The cures were 67.25 per cent, where those that were improved or cured totaled 87.9 per cent.

My technic is ordinarily 200 kv., 20 ma., 50 cm. distance, a tin-copper-aluminum filter, equivalent to 2 mm. of copper; 200 r in air are given weekly for three or four weeks and then, if necessary, carried to a total of 1,000 or 1,200 r at two-week intervals. In cases which have pruritus ani also, it may be of value to administer 100 r anteriorally and 100 r posteriorally at one sitting, crossfiring and allowing the rays to pass through the sacral nerve roots.

Cases apparently of neurogenic origin constitute a large per cent of the total.

Exemplary of this type in my group was a 26-year-old white woman who developed pruritus vulvae et ani three months prior to her divorce. As marital differences increased, itching became intensified to its greatest degree at the time of divorce. This event failed to relieve her pruritus, for by this time she had established a vicious circle of traumatic scratching, producing fissures and lichenification and these lesions in turn caused more severe itching. No skin disease, anal disease, vaginal infection nor uterine abnormality was present. Pruritus was so great that the patient had stayed in bed for two weeks, had slept very little, and was greatly distressed mentally and physically. About four days after the second deep x-ray exposure she was distinctly improved objectively and subjectively. On reporting for the fourth treatment the patient volunteered the information that she had scratched practically not at all in the preceding week and had resumed normal living habits. No symptoms are now present.

Various topical applications had been prescribed without lasting benefit prior to radiation. However, she was placed on other local medicines when under my care to obtain all the help possible from this source. By no means should one fail to use topical medicines, supportive treatment, sedatives and any other measures indicated as an adjunct to deep x-rays.

My experience in treating pruritus vulvae with superficial x-rays has been sufficient to allow considerable observation. However, my experience in treating the same patient first with superficial x-rays, then with deep x-rays, is quite limited. Nonetheless, such restricted observation has been interesting and in most instances the patient apparently has received greater improvement from deep x-rays if their comments are to be accepted.

This report is necessarily confined to seven cases, all of which have been followed. Of this group, six have written that their symptoms were either entirely absent or so slight as to be inconsequential. The seventh case was only temporarily improved; however, this patient received only 700 r. These results cover a period varying from four years in the longest case to two months in the most recently treated.

It seems unwise to attempt the treatment of pruritus incident to leukoplakia and kraurosis vulvae by deep x-rays.

It is hoped that this essay may serve to stimulate more reports in the literature on this subject in order to determine whether others with sufficient clinical material have obtained superior results by means of high voltage x-rays with tin-copper-aluminum filtration as compared to the well-known favorable effects of superficial x-rays.

SUMMARY AND CONCLUSIONS

Attention is called to the scarcity of medical literature reporting the use of high voltage x-rays in treating pruritus vulvae. Such radiation is designed for those cases not due to skin diseases primarily, but to those known as essential, idiopathic or neurogenic in type. A case is cited illustrating favorable results in pruritus vulvae of neurogenic origin following deep x-ray treatment. Observation of the cases constituting this report suggests that superior results have been obtained in idiopathic pruritus vulvae by means of deep x-rays as compared to superficial x-rays. It is agreed that superficial x-rays are sufficient in skin diseases of the vulva. It is hoped that more reports will be made in the literature on the merits of deep x-rays for cases of pruritus vulvae.

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119 North Broadway

DISCUSSION (*Abstract*)

Dr. Franklin B. Bogart, Chattanooga, Tenn.—My experience with this condition is limited and my results have not been very encouraging. However, they parallel those reported elsewhere. Approximately 25 per cent of patients obtained prompt relief, which lasted for a long period. Fifty per cent were slightly to moderately benefited, and 25 per cent received no benefit.

Most cases have had a thorough examination and many special studies in an effort to ascertain the cause of the itching before they are referred to me for radiation. They have usually had a trial of treatment with some of the estrogenic products. If this has not been done, I insist that it be done before radiation or during the time that radiation is being given. Since we do not know exactly why relief is obtained in some cases following radiation, its use is more or less empirical and every effort should be made to eliminate possible causes of the diseased condition.

During recent years, it has been my custom first to try superficial roentgen radiation and, if this fails, to use roentgen rays generated at 200 kv. When roentgen rays generated at 200 kv. were used, my technic has been essentially that of Dr. Eastland. When superficial roentgen rays have been used, I have given a dose of 150 r generated at 85 with no filter or ½ mm. Al. at weekly intervals until 3 or 4 doses have been given unless relief is obtained sooner. I have seldom used radium. I have had very few patients who responded favorably to roentgen radiation generated at 200 kv. who had failed to respond to those generated at 85 kv. If a case by chance had some inflammatory nerve lesion as a basis for the itching, one might expect that 200 kv. radiation would be superior.

Dr. Eastland (closing).—Estrogens are playing a large part nowadays in the treatment of pruritus and can take care of many such cases without radiation. In some of my cases, however, they failed.

SARCOMA OF THE UTERUS*

By WILSON SEARIGHT, M.D., F.A.C.S.
Memphis, Tennessee

Sarcoma of the uterus is a mesoblastic malignant neoplasm arising in the connective tissue or connective tissue derivatives. Up to 1925, Bunten found a total of 352 cases. Since that time a few additional cases have been added.

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*From the Department of Gynecology, University of Tennessee Medical School.

Zacherl estimates that the proportion of non-epithelial malignant tumors of the uterus to carcinoma is as one to forty. Evans reviewed the cases at the Mayo Clinic for the period from 1910 to 1918 and found twenty-two borderline and malignant non-epithelial tumors of the uterus as compared with 873 carcinomas for the same period. Veit, in 42,395 gynecologic cases, found 1,493 carcinomata to forty sarcomata, or a ratio of 1 to 37.2. In a series of 257 malignant tumors of the uterus on the gynecologic service of Mount Sinai Hospital, 236 were carcinomata and 21 sarcomata. Evidently there are great differences in the interpretation of the histologic findings in early or suspicious cases. Some authors include cellular fibroids among the sarcomata. Others bar all but very positive new growths. Thus only can the great difference in percentage be accounted for. The increase in the number of cases reported is most probably due to the systematic and detailed histologic study of the pathologic material rather than to an absolute increase in the number of persons afflicted. Dr. Emil Novak, in his book on gynecologic and obstetrical pathology, published in 1940, says that sarcomas constitute about 4.5 per cent of uterine malignancies. Sarcoma of the uterus is a disease of the climacteric. Masson found an average of 44.86 years in 44 cases. Veit, in a collection of 438 cases, found a few cases in early life, arising mainly from the mucosa, with a rapid increase from the twenty-fifth year up. The greatest number appear between the ages of 45 and 50 years. In 1860, Mayer reported uterine sarcoma to the Berlin Obstetrical Society. Lebert, in 1845, was the first to diagnose this tumor by microscopic examination. In the light of present knowledge, it is quite likely that all cases mentioned in the literature of recurrent fibroids were examples of this tumor. In looking over the textbooks on gynecology, I find very little space devoted to this subject. Its comparative rarity, together with the fact that there are no diagnostic features connected with the disease that render it distinctive, may account for the scarcity of information upon it.

The ancestry of the tumor cells is interestingly discussed in Novak's book. He reminds us that all of the constituent elements of the uterus are of mesodermal origin, and therefore that it would not be surprising if a malignant connective tissue tumor like sarcoma should arise from any of these elements, or for that matter, if at times a mixed tumor should likewise develop, as is actually the case. It is upon a histogenic basis that these tumors are usually classified: first, those arising in the muscle or connective tissue of the uterine wall; second, those arising in myomas of either the corpus or cervix; third, those arising in the mucous membrane of either the corpus or cervix; and fourth, those arising from the blood vessel apparatus. Unfortunately, whatever evidence may present itself from a histologic standpoint, differentiation into the spindle cell, the round cell, and the mixed cell groups is a very serviceable classification. In laboratories with very highly standardized technics, in the preparation of specimens, mytosis counts may be of interest in determining the degree of malignancy, and therefore would be of prognostic importance. Unfortunately, the variation of technic in many laboratories, particularly with regard to the type of fixing, staining and thickness of the sections, renders such a test impractical or uncertain. Where such studies are possible, as in those reported by Evans and Kimbrough, there is a marked parallelism between the degree of malignancy and the degree of nuclear activity.

Certainly an increased number of mitoses suggests rapid growth as well as a susceptibility to x-radiation treatment following operation. Certainly cells undergoing mitoses, in great numbers, are less differentiated than those with fewer mitoses.

The gross appearance of these tumors varies with their origin or histogenesis. Those arising from myomas usually must be distinctly differentiated from myomas with degenerative changes. As a rule, however, the sarcoma is a little bit firmer in consistency and more resembles brain in its gross appearance. Newer types may not prevent any evidence of a pre-existing myoma whatsoever and may cause a symmetrical enlargement of the uterus with the characteristic raw pork appearance on the cut surface that grossly may not be distinguished without cutting through the tumor from a pregnancy. The type arising from the endometrium usually presents a polypoid appearance which may strongly resemble a benign polyp. All types must be subjected to thorough microscopic study in order that this condition may be accurately diagnosed. The etiology of sarcoma is unknown. Stegal and Fox regard sarcoma as furnishing the best grounds for the support of Cohnheim's theory. Trauma and inflammation undoubtedly play some part, either in the production of a lesion from which sarcoma develops or in stimulating certain activity in a latent sarcoma. Experimental implantation of the growth in animals

has been fairly successful, but does not establish an infective character of the disease. Certainly, to date, no specific organism or virus has been isolated or cultured which may be accepted as a cause for sarcoma.

The tumors may be primarily diffuse or primarily circumscribed. This difference in types is apparent only in very early cases. It is quite evident that all will become diffused as the disease progresses. Like carcinoma, sarcoma spreads by metastasis or extension. Those involving the mucosa and cervix spread toward the vagina, while tumors originating as diffuse growths in the uterine wall usually extend through the peritoneal coat and by contiguity to neighboring tissues. Uterine sarcoma occupies a unique position among malignant tumors in that they may grow very slowly or even lie dormant for a number of years and then suddenly, without apparent cause, develop rapidly and metastasize extensively. Metastasis takes place by means of the blood stream. Katz found sarcomatous emboli in the pulmonary vein. The commonest sites for metastasis are the liver, lungs, brain, and retroperitoneal glands. Complications as a result of metastasis are: perforations of the uterine wall by sarcomatous tissue, which may cause peritonitis, fatal hemorrhage, intestinal obstruction, and various types of intestinal fistulae.

Unfortunately the symptomatology of this condition is very vague. Early signs are those of malignancy, namely: hemorrhage, discharge, and pressure symptoms. Associated with fibroids, a sudden increase in the rate of growth is suggestive of sarcoma. Since no definite syndrome is presented, a patient so afflicted usually does not present herself for treatment until extension or metastasis has already reduced her to a state beyond surgical or medical relief.

The prognosis varies with the type of the tumor and the time the diagnosis is made. Slow growing tumors offer the best chance for recovery. Even in these cases their best chances are to have the tumors associated with fibromas so that operation is done incidentally and the sarcoma is found as the result of the microscopic study of the tissue. Treatment for this condition is extensive operation followed by radium and x-ray therapy. Theoretically, there is a time when every sarcoma of the uterus is curable. From a practical standpoint, however, we have found no case that came to us early enough, with a diagnosis made, where operation and radiation would avail us of any cures. The chaotic state of affairs of this subject has prompted me to present this subject to you with the hope that suggestions may be made in the discussion that will lead us to diagnose this condition earlier and therefore permit a greater salvage of cases.

The following study comprises a survey of the work done between the years 1929 and 1939 in the John Gaston Hospital. In the ten-year period 8,786 gynecologic cases were discharged from the hospital. Of this number 3,202 were fibroids. During this same period there were 576 carcinomas of the uterus. The classification of these carcinomas, according to situation, was as follows: twenty-five were carcinomas of the body of the uterus, 551 were carcinomas of the cervix, and this same period gave us a total of twelve sarcomas. Thus we see that fibromas made up 35 per cent of the total number of cases treated on our service during the ten-year period. Uterine malignancies made up slightly over 6 per cent of all our admissions. Uterine neoplasms of all descriptions numbered 3,778, and 84 per cent of these neoplasms were fibroids. In all, a total of 3,790 uterine neoplasms were included in this period of time. Our percentages in classification of this number are as follows: eighty-four and nine-tenths per cent were fibroids, 14.53 per cent were carcinomas of the cervix, 64 per cent were carcinomas of the body of the uterus, and 0.03 per cent comprises our series of sarcomas. There were 588 cases of malignancy of the uterus; 551, or 93.7 per cent, were carcinoma of the cervix; 25, or 4.4 per cent, were adenocarcinomas of the body of the uterus. There were twelve sarcomata, or 2 per cent of the total number of malignancies. Comparing this with Novak's statement that sarcomas comprise 4.5 per cent of all uterine malignancies, our observations are that the incidence, on our service, is less than one-half of this figure. This may be accounted for by several factors. First, the length of time over which the study is made may not be long enough. Second, we have not been on the lookout for this tumor, so that many cases that were classified as fibromas probably contained some carcinomatous change that was not recognized. Our ratio of sarcoma to other uterine malignancies is one to fifty-three as compared to Veit's figures of 1 to 37.2. Zacherl's observations more nearly compare with ours, since he says that non-epithelial malignant tumors of the uterus, as compared to carcinoma, is as 1 to 40. The highest incidence of sarcoma was obtained from the figures from Mount Sinai Hospital, where there were twenty-one cases out of 236 uterine malig-

nancies, a percentage of 8. Our series of twelve cases revealed the fact that eleven were colored and one was white. The oldest was 69, the youngest 45, an average age of 53.3 years. Six of these patients had never been pregnant. One patient had had six children. Three more had had one each, and one had had three. Under the head of chief complaint we find that bleeding occurred in eight of the twelve patients. Strange to say, foul discharge was present in only three of the twelve cases. Tumor was noticed by the patient in nine cases. Lengths of time the tumor had been noticed varied from one week to thirteen years. Rapid loss of weight was complained of by only two patients. One patient said that she had lost one hundred pounds in four months. Another case complained of losing forty pounds over a period of eight months. Only two cases presented a red blood count of less than 3 million, one being 2,480,000 with a hemoglobin of 5.9 grams and the other 1,810,000 red cells with 7.5 grams of hemoglobin. The remaining cases did not show any marked secondary anemia whatsoever. All cases complained of weakness except one. The weakness varied from marked to very mild, but was present probably with the greater consistency than any other symptom complained of. At operation, gross evidence of metastasis was noted in six cases. One case did not come to operation. The diagnosis was made from a biopsy of the cervix and there were other evidences of metastasis which placed the patient in the category of hopeless. All authorities agree that the operation of choice in these cases is panhysterectomy. It was possible in only three cases. Six cases had supravaginal hysterectomies. In one case left salpingectomy and right salpingo-oophorectomy was done and one case was described as being inoperable. Seven cases were described as difficult, with the presence of friable tissue and much bleeding. One case was diagnosed by biopsy alone and no operation was done because it was apparently hopeless and inoperable. The next case was explored and found to be inoperable and a biopsy of the omentum revealed the diagnosis. Five cases had a good postoperative course. Diagnosis was confirmed by histologic study in all cases. One case was interesting in view of the fact that there was a coexisting polypoid adenocarcinoma in the uterus, in addition to myosarcoma. The literature further indicates that radiation, following radical operation, is the treatment of choice. Only three of our cases were given postoperative radiation. Our follow-up shows that, with the exception of two cases, all have died. One could not be traced. Of the cases that are living, both were operated upon late in 1939. This is, of course, too short a time to determine whether these cases will survive.

Summarizing the information revealed from this study, several things are quite noticeable. First, there are no diagnostic symptoms of sarcoma of the uterus. At least we know of none to date. Second, our experience seems to point to the fact that the ideal treatment, namely, panhysterectomy followed by radiation, can be carried out in only a few cases. This is due to the fact that by the time the cases present themselves for treatment they are already hopeless. This subject is presented with the hope that it will recall to our minds the possibility of the existence of the disease, and that if we consider the possibility of its existence we shall advise operation earlier in cases associated with fibroid tumors. Our experience has not been encouraging. It would seem that in a service as large as ours we could diagnose these cases earlier. However, we have not been able to do so and our salvage has been nil or extremely small. The symptomatology is not characteristic enough to be pathognomonic unless the disease is suspected. Irregular bleeding and marked weakness were characteristic of all of our cases. It would be foolish to say that these symptoms indicate sarcoma, for many other conditions can produce them. The history of rapid growth of a pelvic tumor, plus bleeding and weakness, is certainly suggestive. Bearing in mind the possibility of sarcoma and combining that with a good history and physical examination, may lead to earlier diagnosis in the future.

DISCUSSION (*Abstract*)

Dr. Emil Novak, Baltimore, Md.—Sarcoma of the uterus is so much less common than carcinoma of the uterus that it has received far less attention. And yet it is a very interesting lesion and not exceedingly rare.

Some years ago we made a study of our own cases for a period of twenty-five years, and found that in something like 27,000 case specimens we had 59 cases of sarcoma of the uterus. It is therefore not a very common disease, but it is sufficiently common so that we should all be on the alert for it.

Dr. Searight expressed disappointment at his failure and the failure of his colleagues in not being able to make diagnoses beforehand, but I do not think he need feel that way about it, because there are no very important diagnostic criteria in a great majority of cases.

If a myoma of the uterus grows rapidly during reproductive life, one can think about the theoretical possibility of sarcoma, but there is usually no accurate way

of making the diagnosis. Curettage will often fail to help us; occasionally it will, where the tumor has ulcerated into the uterine cavity. Somewhat more frequently we may encounter suggestive signs after the menopause. If a myoma after the menopause, when it should ordinarily retrogress and not grow, begins to grow rather rapidly, with bleeding as a symptom, we again have a right to suspect the possibility of sarcoma, but we will not always find it.

Postmenopausal bleeding of this sort is more apt to be due to carcinoma of the fundus; nevertheless we should be on our guard for the possibility of sarcoma. Sarcoma of the uterus can arise in any of the connective tissues of the uterus.

The type in which clinicians are most interested is that which develops in previously benign myomata. This does not happen nearly as commonly as was at one time believed. At one time its incidence was given as high as 10 per cent, because many cases were called sarcoma which were merely richly cellular but perfectly benign myomata of the uterus. Definite criteria of malignancy must be present before we are justified in making the diagnosis of sarcoma.

Disparity of cells, hyperchromatosis and mitosis must be seen. The latter is very important not only in diagnosis, but in evaluating the tumor from a prognostic standpoint, as Dr. Searight has said. I do not mean to say, when I emphasize mitosis, that unless you find mitosis in an individual section you cannot diagnose sarcoma, because that is not true.

From a practical standpoint, the type of sarcoma that develops in myoma is often very important. In going over our material of previous years, for example, we not infrequently encountered cases in which a tumor had been removed, on the assumption that it was a perfectly benign myoma, and I am sure that almost every surgeon has had that experience.

Supravaginal hysterectomy is often done in such cases, with conservation of the ovaries, and then the laboratory comes with the report that sarcoma is present, putting the surgeon in a quandary. Each case must be individualized but, in the main, the better plan is to treat such a case not with further operation, but with radiation.

When metastasis occurs in a sarcoma, it is just as apt to be seen in some distant organ, like the brain or the lungs, as locally, and the extra hazard of doing a second operation shortly after the first would not be counterbalanced by the relatively slight degree of protection it would offer the patient.

So that, in the majority of cases, especially when the amputation has been well below the level of the tumor, as it generally is, it is much better to depend upon radiation. As a matter of fact, some of these patients do not have the benefit of any postoperative radiation and still remain perfectly well.

The type of sarcoma which develops in a myoma can be relatively benign or it may be very malignant. The sarcoma which develops in the general musculature of the uterus is usually very malignant and sometimes metastasizes very rapidly. It is not always easy to tell at the time of operation whether a tumor has arisen from a myoma or whether it has arisen in the general musculature.

We must remember, for example, that many sarcomas have a tendency to grow in a nodular fashion, though. Sometimes they are quite symmetrical, resembling a pregnant uterus. When nodular one may wrongly assume that the sarcoma has arisen from a myoma.

Another practical point is that sometimes one can form a suspicion of sarcoma from the gross appearance of the tumor. The practical point is that every tumor should be cut into before the abdomen is closed. If it presents the hard, glistening, whorl-like surface characteristic of myoma, one does not have to think much about the possibility of sarcoma. But if one finds pultaceous areas with ragged cavities, one ought always to suspect sarcoma. Certain types of hyalin degeneration may resemble sarcoma superficially, but usually with hyalin degeneration the surface is more amorphous with a tendency to liquefaction.

Frozen sections are sometimes helpful, but usually not. They are not nearly so valuable in the diagnosis of these connective tissue tumors as they are in the diagnosis of the epithelial types, but if one finds a definitely suspicious picture, one would be inclined in most cases to do the radical operation.

Some time ago I operated upon the wife of one of my colleagues for a large myoma. When we opened it, it had a suspicious appearance. I did the complete operation. She received postoperative radiation because we found sarcoma in the sections, but she was dead inside of eight months with metastasis of the brain.

Our five-year salvage in our 59 cases, which I think is the largest series that has been reported, was only 24 per cent, something like that of cervical sarcoma in general. The cases that develop in myomata, generally speaking, are apt to be less malignant than the diffuse variety.

Finally, a word about another type of sarcoma of the uterus which may be readily overlooked, and that is the type that comes from the endometrium. As Dr. Searight has said, sarcomas of the endometrium tend to assume a polypoid form. If we open a uterus and find it contains large polypoid masses, is bulky and friable in appearance, we ought always to suspect sarcoma, and the same statement may be made with reference to cervical polypi which are unusually solid and friable.

Dr. Searight (closing).—Recently some work has been published about the biological diagnosis of malignancy wherein the rate of the digestion of fibrin in the blood is determined. The number of false positives and the number of false negatives in this test have not yet rendered it very serviceable, but it is hoped that research work along this line will enable us to diagnose malignancy of all types soon. If this were possible, I should place the treatment of sarcoma in reverse position; that is, if it can be diagnosed before operation, radiation first, followed by operation, would seem to me to be the most rational way of handling the cases.

When I chose this subject for a paper it was because of the fact that we had done nothing for this type of case. A search through the literature did not enlighten me very much.

I have enjoyed the study of it, and I have been refreshed by Dr. Novak's discussion, but it would seem that the condition is still one that looks rather bad. It is a hopeless condition if not treated correctly and soon enough.

THE USE OF ERYTHROL TETRANITRATE AS A DIURETIC*

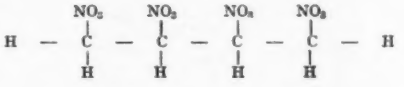
By WILLIAM M. NICHOLSON, M.D.
and
VINCENT E. MOSELEY, M.D.
Durham, North Carolina

The purpose of this report is to call attention to another action of a drug that over a long period has been used clinically for other purposes. Erythrol tetranitrate was first prepared and used clinically by Bradbury[1] in 1895. Recognizing the desirability for a vasodilator whose action would be prolonged over that of the nitrites and nitroglycerin, he nitrated several of the lower alcohols; among them was methyl nitrate, glycol trinitrate, glycerol trinitrate, erythrol tetranitrate and mannitol hexanitrate. Observing the effect of these various substances in perfusion experiments and on patients, he came to the conclusion that erythrol tetranitrate was the most practical one to use. He recommended that it be used in

"a condition in which the heart is laboring under increased work imposed upon it by contracted vessels."

Likewise he said that erythrol tetranitrate was not a diuretic. A careful search of the literature fails to reveal any reference to the fact that the drug has any diuretic action. It is to be noted, however, that as early as 1679, Thomas Willis[2] used potassium nitrate in the treatment of dropsy. Many writers since then have advocated the use of potassium nitrate in patients with edema. Among the most recent were Keith and Binger,[3] but it must be noted that they were primarily interested in the potassium salts rather than the nitrates.

Erythrol tetranitrate is a white, bitter tasting odorless salt obtained by nitrating the low alcohol erythritol, having a structural formula as follows:



It is dispensed in compressed tablets containing 32 mg. each. It is administered orally and as used in these experiments the dose varies from 96 to 160 mg. each day. No effect on the urinary excretion is observed until 2-4 days have elapsed. We have observed only a minimal effect upon

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*Read in Section on Medicine, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Department of Medicine, Duke University School of Medicine.

*We wish to express our thanks to Dr. W. A. Feirer, of the Sharp & Dohme Co., Philadelphia, for the lyophylized serum used in Case 1. Our thanks are also due to Dr. W. J. Henry, of Chester, South Carolina, for the record kept on one of the cases reported.

HISTORY NUMBER	AGE	RACE	SEX	DISEASE	B.P.	URINE		PLASMA		BLOOD		OTHER DIURETICS	RESULTS	RESULTS AFTER ERYTHROL TETRANITRATE (GRAMS NURSED BETWEEN 90 AND 100 MEAL A DAY)
						R.B.C. P.H.F.	ALBUMEN	TOTAL PROTEIN GMS. PER 100 C.C.	ALBUMEN GMS. PER 100 C.C.	NON-PROTEIN NITROGEN MGM. PER 100 C.C.	CHOLESTEROL MGM. PER 100 C.C.			
A-13156	33	W	F	NEPHROTIC SYNDROME	138/98	2-4	++++	3.8	1.0	64	486	AMINOPHYLLIN POTASSIUM CITRATE POTASSIUM NITRATE DEXTROSE 50% ACACIA UREA	NO CHANGE NO CHANGE NO CHANGE NO CHANGE NO CHANGE SLIGHT DIURESIS	GIVEN 2-3 WEEKS BEFORE DEATH. NO DIURESIS COURSE OF DISEASE PROGRESSIVE. DIED IN UREMIA
85135	27	C	M	NEPHROTIC SYNDROME	112/70	4-8	+++	4.1	1.2	31	529	THYROID UREA	DIURESIS LOSS OF 4 KILOS IN 7 DAYS. 5 KILOS. IN 6 DAYS. NO CHANGE	DIURESIS LOSS OF 4 KILOS IN 7 DAYS. RECURRING EDEMA CONTROLLED BY ERYTHROL TETRANITRATE.
A-13316	18	W	F	NEPHROTIC SYNDROME	150/90	3-10	++	4.0	1.5	89	436	DEXTROSE 50% SUCROSE 50% DIGITALIS THYROID AMINOPHYLLIN THEOCIN TRANSFUSIONS	NO CHANGE NO CHANGE NO CHANGE NO CHANGE NO CHANGE NO CHANGE NO CHANGE	DIURESIS WITH LOSS OF 10 KILOS IN 24 DAYS. MARKED IMPROVEMENT FOR ONE YEAR. DIED IN UREMIA AFTER PNEUMOCOCCUS PNEUMONIA.
63431	22	W	M	NEPHROTIC SYNDROME	114/78	OCC.	++++	3.6	2.2	42	450	LYOPHYLIZED SERUM 900 C.C.	NO CHANGE	DIURESIS WITH LOSS OF 12 KILOS IN 23 DAYS. COURSE OF DISEASE PROGRESSIVE. EDEMA LATER DEVELOPED THAT DID NOT RESPOND DIED IN UREMIA 14 MONTHS AFTER ONSET
A-32771	18	W	M	NEPHROTIC SYNDROME	140/90	4-10	++	3.8	1.3	36	310	AMINOPHYLLIN	NO CHANGE	DIURESIS WITH LOSS OF 6 KILOS IN 14 DAYS. RECURRING EDEMA CONTROLLED BY ERYTHROL TETRANITRATE
A-37338	49	W	F	NEPHROTIC SYNDROME	140/80	OCC.	+++	4.3	1.4	33	572	POTASSIUM CHLORIDE THYROID	SLIGHT DIURESIS SLIGHT DIURESIS	SLIGHT DIURESIS NO WEIGHT LOSS
A-38860	21	W	M	NEPHROTIC SYNDROME	128/80	50-100	+++	3.8	1.4	40	386	TRANSFUSION, SERUM TRANSFUSION, WHOLE BLOOD	NO CHANGE NO CHANGE	NO DIURESIS. STEADY GAIN IN WEIGHT. COURSE OF DISEASE PROGRESSIVE. DIED IN UREMIA 3 MONTHS AFTER ONSET
A-43529	31	W	M	NEPHROTIC SYNDROME	132/80	5-20	+++	3.8	1.8	30	540	BED REST ONLY	MARKED DIURESIS LOSS OF 9 KILOS IN 10 DAYS	REACCUMULATION OF EDEMA AFTER DISCHARGE MARKED DIURESIS LOSS OF 7 KILOS IN 21 DAYS NOT AT BED REST
37829	61	W	F	MYXEDEMA	92/68	0	0	5.5	—	—	510	THYROID	MARKED DIURESIS	SLIGHT DIURESIS. GAIN IN WEIGHT. NO IMPROVEMENT UNTIL THYROID GIVEN
A-41819	53	W	M	CIRRHOSIS OF LIVER, GLOMERULO-NEPHRITIS	140/106	50-100	++++	5.8	2.9	38	225	UREA	NO CHANGE	NO CHANGE

Table 1
Comparison of erythrol tetranitrate with other diuretics.

the blood pressure of the patients studied and for that matter patients with hypertension have shown little or no fall in the blood pressure. For further pharmacologic actions one is referred to the studies of Krantz and his co-workers.[4]

The only toxic effect that we observed with the use of erythrol tetranitrate was the occurrence of a rather severe, dull, generalized headache. The headache, however, was promptly relieved when the dosage of the drug was reduced.

MATERIAL

Eight patients with the nephrotic syndrome of subacute glomerulonephritis have been studied, and as a control the drug was given to one patient with myxedema and one patient with portal cirrhosis of the liver and acute glomerulonephritis. Patients in cardiac failure with edema are not included since the diuretic effect of bed rest and digitalis would allow no critical estimation of the value of erythrol tetranitrate; however, it may be stated that the drug has been given many times in this condition.

The patients were placed on an adequate diet that contained approximately 1 gram of protein per kilogram of body weight. An effort was made to restrict the sodium chloride intake in the diet. However, no special precautions were carried out in the preparation of the food. The fluid intake was limited to 2,000 c. c. In most instances the patients had been at complete bed rest. However, following discharge from the hospital, they have been ambulatory and have continued taking the drug.

Other diuretics were administered to the patients before erythrol tetranitrate was given, and an attempt was made to allow several days to elapse after one diuretic was stopped before another was given. This precaution was not always possible. In no instance were the mercurial diuretics administered.

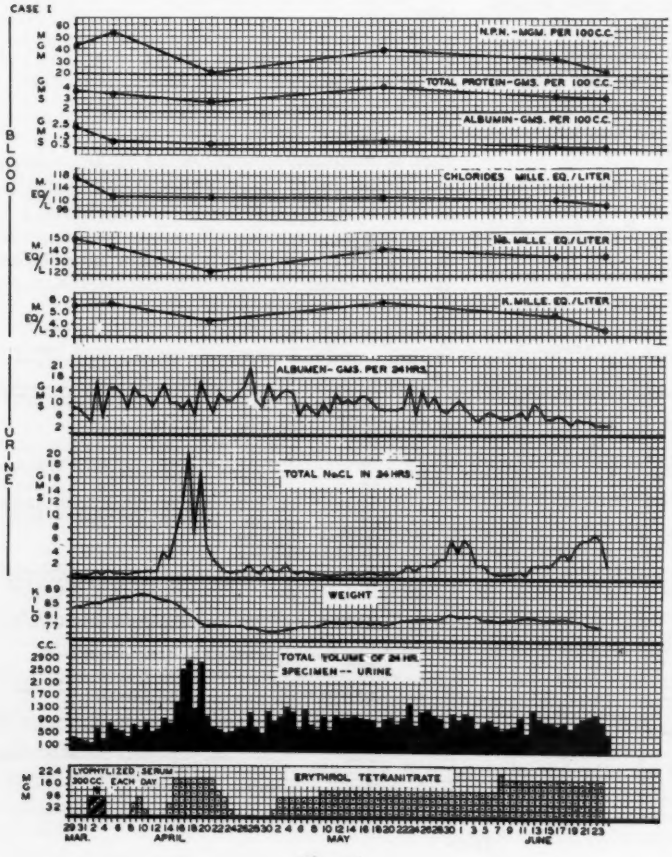

Chart 1

Case 1 (*History 63431*).—A 22-year-old white male student, who two years previous to the present admission had rather severe ulcerative colitis, apparently had made a satisfactory recovery from this illness. Two days before admission he noticed puffiness beneath the eyes and some edema of the ankles. The physical examination revealed little of interest except for the generalized soft, fluffy, pitting edema. The blood pressure was 114/78. The eyegrounds were entirely normal. Proctoscopic examination and barium enema showed no abnormalities. The urine contained a considerable quantity of albumin, waxy casts, doubly refractile bodies and only an occasional red cell. There was moderate anemia. The concentration of various chemical elements in the blood is summarized in *Chart 1*. On the fourth hospital day the patient was given lyophylized human serum intravenously equivalent to 300 c. c. of normal serum.[5] This was given for three days for a total of 900 c. c. equivalent. No increase in urinary flow re-

sulted from this procedure. There was no change in the proteins of the patient's serum. Four days were allowed to elapse and the patient was given erythrol tetranitrate. A slight increase in urinary output was noted and the drug was discontinued for three days. Upon resumption of the administration of the drug three days after it had been discontinued, the patient experienced a marked diuresis, with corresponding loss of weight. It is interesting to note that there was an increase in the urinary excretion of sodium and chloride, and the concentration of these ions in the urine was increased. The patient maintained a satisfactory urinary excretion while in the hospital with no reaccumulation of edema. After discharge he developed edema, which was not controlled by erythrol tetranitrate. He died 14 months after the onset, in uremia.

Case 2 (*History 13316*).—A 16-year-old white girl four years before admission had an attack of acute glomerulonephritis which necessitated her remaining in bed for seven months. Between that time and two months before this admission she had had repeated upper respiratory tract infection associated with edema of the legs. Two months before she had the onset of nocturia, hematuria, dyspnea and edema, which had progressed to the time of admission. The physical examination revealed hemorrhages in the right optic fundus, signs of right hydrothorax and ascites. The heart was slightly enlarged to the left; however, no other signs of cardiac disease were elicited. The blood pressure was 150/90. The urine showed the specific gravity to be fixed at 1.012, four plus albumin, there were many white cells, 3-4 red cells and an occasional hyaline and waxy cast were seen in the sediment. The chemical findings are given in *Chart 2*. During the first 41 days in the hospital the course of the disease progressed. Erythrol tetranitrate was given to the patient and on the third day there was a diuresis which continued for the remainder of her hospital stay. She was discharged from the hospital edema-free, with marked clinical improvement. She was readmitted to the hospital 14 months later with pneumococcus pneumonia that had been contracted 15 days previously. She died from a combination of the pneumonia and uremia.

Case 3 (*History A-38860*).—This 21-year-old white male student was admitted to the hospital complaining of generalized edema of one month's duration. Two months before the appearance of the edema he had been confined to the infirmary for ten days with an upper respiratory tract infection. Eight months before entry a trace of albumin had been found in his urine. The physical examination revealed extensive brawny edema of the entire body. The eyegrounds were normal, the blood pressure was 132/80. The urine contained 3 plus albumin, cellular and waxy cast and occasional red cells. Doubly refractile bodies were demonstrated in the urinary sediment. The blood chemical findings are summarized in *Chart 3*. After eight days of hospitalization the patient was given erythrol tetranitrate. There was no response to this drug in any way except that after ten days he developed a severe generalized, dull headache. The course of the disease was progressive and he died in uremia approximately two months after admission to the hospital.

RESULTS

Eight adult patients with the nephrotic syndrome of subacute glomerulonephritis have been studied. In six of these patients, diuresis was obtained so that all clinical evidence of edema had disappeared. Likewise there was improvement in the subjective symptoms of these patients. Three of them showed a diuresis after one or several other diuretics had failed to pro-

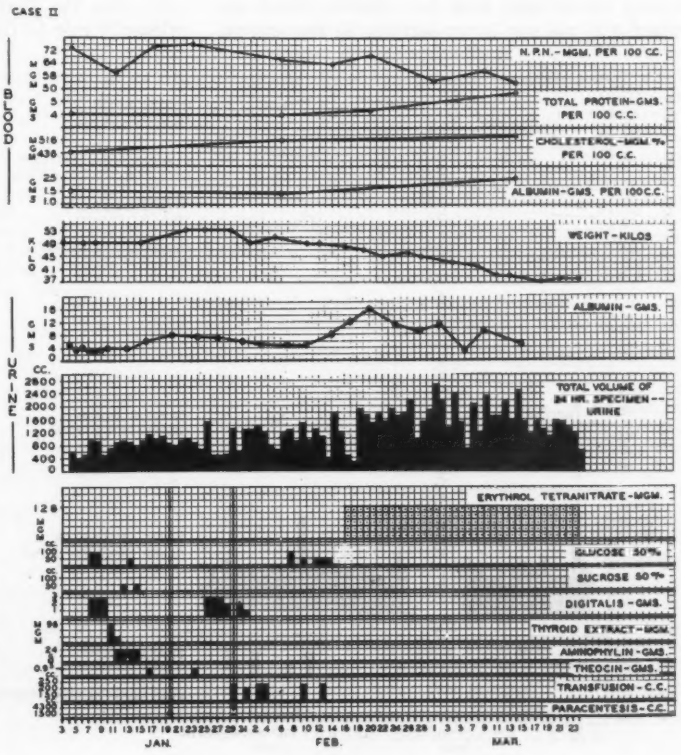

Chart 2

duce this response. One patient responded to erythrol tetranitrate as well as to two other diuretics that had been tried previously. Diuresis was obtained in one patient while ambulatory. A case of myxedema was studied in which there was an increase in the urinary output, in spite of which there was a gain in weight. We do not believe that erythrol tetranitrate had any effect in the case. A patient with cirrhosis of the liver and acute glomerulonephritis showed no response.

DISCUSSION

The mechanism of the diuretic effect of erythrol tetranitrate is not known and any theories propounded at this time to explain the phenomenon would be highly speculative. In general, a diuretic may act in one of three ways. It may change the composition of the plasma, increase the volume of glomerular filtrate or decrease the reabsorption in the tubule. No significant change in the plasma proteins was found in any of the patients studied and from this fact it may be assumed that any diuretic effect obtained was not due to an increase in the onconic pressure. This statement is made with certain reservations, however, since an analysis of the various components of the plasma was not made in every case.

Herrick, Mann and Sheehan,[6] by means of a thermostromuhr unit, were able to demonstrate an increase in the blood flow through the kidney after amyl nitrite had been given to dogs. The effect was quite transient, however. Chasis, Ranges, Goldring and Smith[7] found that in man the plasma flow and filtration rate were decreased after amyl nitrite by inhalation and sodium nitrite by intravenous infusion had been given. In fact, after approximately three hours there was marked oliguria. They also presented evidence to show that the tubular activity was not impaired. It must be noted that the effect obtained by them was on a subject whose kidneys were presumably normal; also that the experiment lasted only a few hours. As pointed out previously, no increase in the urinary output was noted for 2-3 days in the patients presented in this communication. It would appear, however, that the diuretic effect obtained was not primarily due to the nitrates as such, but probably in combination with the alcohol or perhaps the alcohol itself was responsible. Further studies are being carried out with the hope of throwing some light upon this.

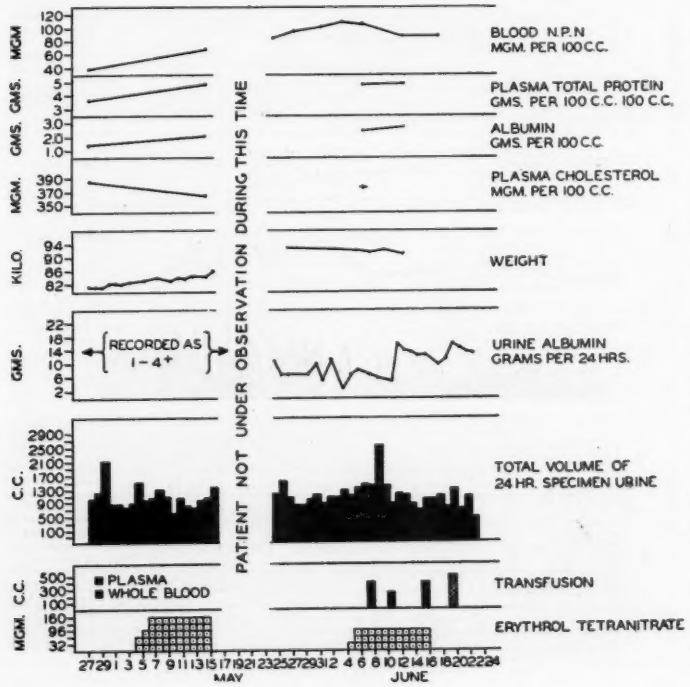

Chart 3

In the consideration of the two patients who failed to respond to the drug, we believe that the involvement of the kidneys was too advanced, leaving little or no normal tissue to act. Peters[8] has pointed out that diuretics do not cause either a chemical or biological revolution in the body, but work through existing physiologic mechanisms. In both cases that failed to respond, the disease was progressive and renal function studies that we were able to perform indicated that only a small amount of functioning tissue was left.

Emphasis must be placed upon the fact that

erythrol tetranitrate or any other form of therapy had no effect upon the course of the disease. Four of the eight cases studied died later in uremia. We do not believe that erythrol tetranitrate prolonged the life of the patients or hastened the death in any instance. If by further studies it can be shown that the drug increased the blood flow through the kidney, it would seem that this fact might play an important role in the healing process. However, such proof at the present time is lacking.

From the experience presented here it would seem that erythrol tetranitrate is as efficient as any other diuretic and carries with it less danger than some of them. In the use of any diuretic it must be remembered that the treatment is directed at only one symptom of the disease and not toward the fundamental changes that have taken place in the body.

SUMMARY

Eight patients with nephrotic edema have been presented, six of whom gave a diuretic response to erythrol tetranitrate.

The diuretic effect was obtained only after the drug had been given for two to three days.

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DISCUSSION (*Abstract*)

Dr. Virgil E. Simpson, Louisville, Ky.—In the "English Dispensatory" by James, published in 1747, under the subject "nitre," one finds the preparation "dulcified spirit of nitre" described as the famous lithontriptic used by Sylvanus and that it "provokes urine." In Stokes' "Theory and Practice of Physic," published in 1840, one reads: "An increase of the secretory function of the kidneys will afford relief in fever" and that "spirits of nitre will be serviceable." The French chemist Balard, in 1844, produced amyl nitrite and Lander-Brwnton in 1869 reported his experiments, concluding that the drug dilated the peripheral arterioles, as could be demonstrated on ear vessels of rabbits, and he further believed it acted on vasomotor centers. Hoffman, in 1872, reported on the glycosuria from its use and commented on "the great increase in amount of urine" following its administration. Brocklesby wrote in 1862 that he habitually prescribed an ounce of potassium nitrate daily for "renal dropsy."

In the chapter on "Diuretics" H. C. Wood, Jr., in his book, "Materia Medica, Therapeutics and Toxicology," published in 1875, said: "Mere vascular fulness tends to provoke excretion of water by the kidneys," and then he goes on to say this statement does not rest on theory and quotes from what he calls "an elaborate series of experiments by Roux" to prove it. He then lists sweet spirits of nitre as a hydrogogdiuretic, says it has decided diuretic action, but not powerful enough to make it valuable in dropsy.

The literature of today confirms a fairly long clinical experience with the nitrite group as symptomatic relief agents in that rather sizable portion of the anguinal group apparently dependent upon a spasm of the coronary vessels. In this particular class relief is obtained by any member of the nitrite order. Their relative value is determined by the rapidity of action and may be ranged as amyl nitrite, the speediest, and erythrol tetranitrate, the slowest. And the members of the list maintain this relative position when the duration of action is considered. If, then, relief in angina due to paroxysmal ischemia comes from a dilatation of blood vessels, one may, by analogy, turn to the kidneys with an understandable mechanism of the diuresis that not infrequently follows their use. By that analogy, when an unusual vasomotor tone obtains in the renal vessels, the water output will be lessened and the administration of any member of the nitrite group will acquire the label "diuretic." The time action which determines their relative value in an anginal syndrome also determines their relative value as a diuretic, but in reverse order. Now the slowest acting member will necessarily rank higher in promoting water loss than one with a time action beginning in one or two minutes and lasting only an hour, as is true of nitroglycerine. Yet even with this evanescent action it is a common knowledge that diuresis follows a dose of nitroglycerine in an anginal seizure not dependent upon an atheroma of the aorta.

The vessels of the Malpighian tufts would seem to be the logical site of action of the whole nitrite group, including tetranitrate. This thought is buttressed by recalling the pharmacological antagonists of the nitrite group. All drugs that raise arterial tension, cause contraction of blood vessels and lessen the blood supply to a structure are antagonistic. As they are useless in

angina due to sclerosis of vessels of the heart, so will they fail to dilate the renal vessels when sclerosed, and hence cause no diuresis.

Some of the nitrates undergo reduction into nitrites and act as true nitrites. Nitroglycerine is an example. Erythrol tetranitrate is another. Being a nitrate, it must be converted into a nitrite before any effect is noted upon blood vessels. The major difference in these two drugs is in the time required for the reduction to take place.

Many authors refer to anuria as does the essayist. The explanation is, I think, that when the vessels are too much contracted to permit maximal excretion, these drugs dilate them and diuresis will follow. But if the vessels are already of normal caliber and this caliber is the optimal, a nitrite may then lessen excretion by lowering general blood pressure.

Bradbury's observation that erythrol tetranitrate had no diuretic action is no more conclusive than Withering's observation that digitalis was a diuretic; he overlooked its cardiac action. It is not probable that the action of the nitrate group depends upon an alcoholic content. Alcohol does not enter into the manufacture of potassium nitrate; it does with sweet spirits of nitre and amyl nitrite. Depression of the vasomotor mechanism is an action common to the whole group. The dilatation occurs even if the spinal cord is destroyed; it occurs after degeneration of the cervical ganglia; the depression does not result in paralysis because stimulation of the splanchnics will cause a rise in blood pressure; the dilatation is not the result of a central action because if a nitrite is introduced into the cerebral circulation but prevented from reaching the general circulation, the blood pressure will not fall.

Dr. Nicholson (closing).—There was really no change in the blood pressure in these individuals, and I do not think that it is of a great deal of use from the standpoint of lowering of pressure in the circumstances.

As to dosage, by the method of trial and error we started with a half grain three times a day, usually before meals, and if no diuresis occurred in the next two days the dose was stepped up to a grain three times a day, and I think that the patients themselves will stop you and not let you get too far in the dosage because of the intense headaches that they have. In most of these, two and a half grains were used.

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EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
Thirty-Fifth Annual Meeting
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CORPUS LUTEUM AND ANESTHESIA

A somewhat unexpected action of a hormone, according to Selye,[1] of McGill University, is its anesthetic effect. In studying the steroid hormones, which include those of the adrenal cortex, ovary and testis, he noted that it was very difficult to produce symptoms of overdosage from subcutaneous injections of oily solutions of any of them, even if enormous quantities were given. He believed it might be due to the slow absorption.

The materials were absorbed much more rapidly if given intraperitoneally, and were more quickly active. If intraperitoneal injections of 35 milligrams of progesterone (corpus luteum hormone) or desoxycorticosterone (adrenocortical hormone) were administered to rabbits, within fifteen minutes all the females were deeply anesthetized and a number of the males showed some degree of anesthesia. The animals which received the same quantity of ovarian follicle hormone (estrogen) showed no anesthesia. All the females died following this high dosage, as did some of the males.

Smaller doses could be used without apparent harm for surgical anesthesia; and after recovery from the anesthesia the animals exhibited no ill effects. Blood pressure[2] during progesterone anesthesia was not lowered more than it is under a barbiturate; the anesthetic effect was unrelated to a depressor action of the hormone.

These results should add something to the understanding of the mechanism of loss of consciousness.

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FOOD AND LONGEVITY

According to archeologists, Indians who were meat eaters in America several hundred years ago were freer from arthritis and dental caries than were the agricultural tribes. The advantages of high and low protein diets have been intensively investigated by biochemists since the birth of biochemistry. Chittenden, early in this century, from work with college students, advocated a low protein diet. Proteins were believed by many to cause auto-intoxication. With the intensive vitamin studies of the past 25 years, the emphasis has swung to supplying an abundance of the accessory food factors, and upon the disastrous effects of their absence to young animals. Sherman noted some years ago that vitamin G deficiency brought about an early appearance of aging in animals and various workers have reported that abundant milk in the ration increases longevity. However, longevity on the whole has not received a large amount of biochemical consideration.

Investigators[3] at Cornell have systematically studied the effects of several dietary variations upon the length of life of rats, with emphasis upon the differences brought about by high or low protein. The experimental diets were begun after the animals had reached middle age. Both the type of protein and its amount, exercise, and restriction of the total quantity of the ration were studied as to their effects upon the duration of life of the animals and the condition at death. Highly purified food materials were used, with sometimes milk proteins and sometimes liver as the source of protein.

The rats which received their protein as liver outlived those fed casein and lactalbumin, the milk proteins. Rats restricted in the quantity of their food and thus kept thin, lived longer than those which were permitted to eat as much as they wished and grow adipose. The hearts

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of those fed the high liver diets were heavier than those which received a lower per cent of liver. The kidneys were enlarged on high protein rations and were heavier in the animals which had been exercised. The livers were heavier on the higher protein levels and the testes were notably heavier. The animals upon low protein rations lived longer.

The important factors during the latter half of life, in influencing the life span, seemed to be the factors which influenced the fatness of the body. Animals restricted in the quantity of their food intake, other things being equal, lived longer than those which ate all that their appetites directed. Exercise after middle life was not uniformly beneficial, but excess weight uniformly increased the death rate.

The statistics thus experimentally obtained, of course, are in agreement with those long publicized by life insurance companies to the effect that thin persons outlive the stout after the age of 40. The question of whether liver proteins are better than milk proteins is a very complex one. Liver is the source of many valuable food materials other than protein, and also of many types of protein, whereas the Cornell workers were comparing it with two isolated proteins, purified from the accompanying substances of milk. Perhaps merely a greater variety of proteins is beneficial, regardless of their source. Modern nutrition work deals with increasingly highly purified foodstuffs and usually a so-called high protein diet refers to one high in a single protein. It is not comparable to the variegated high meat or vegetarian diets which were formerly studied, and which man is likely to consume.

Studies upon highly purified rations are very informative and provide an alphabet in all senses of the word for work in human nutrition. However, because animals with 10 per cent casein or 10 per cent liver live longer than those with 40 per cent of each, respectively, one may not generalize that man should stick to a low protein diet and cut down on eggs, meat and milk. Too many variables are involved. First, the other components of the rat diet were as simple as nutritional scholars could make them. Prolonged meat eating of explorers in the Arctic has not shown deleterious effects.

Meat is difficult to preserve and difficult to obtain both in civilized and uncivilized communities. Agriculture provides more immediate social security and a cereal diet has spread with civilization. This does not prove its greater healthfulness. Although much is now known about the optimum ration for men, in a way the ground has hardly been scratched.

The rat has long proven useful as a guide in work upon human nutrition, because his ration is very nearly like that of man. It is interesting that he confirms established beliefs about the optimum human requirement and statistical evidence of life insurance companies, that the fat, like the good, die young.

VITAMIN E DEFICIENCY

It is characteristic of vitamins that they are almost as specific in their effects as are enzymes, and the enzyme is believed to fit a reaction like a key into a lock. Treatment with vitamin A never cures beriberi, but always xerophthalmia; only vitamin C cures or prevents scurvy, and so on. Increase or aggravation of symptoms of one deficiency following administration of concentrated doses of another vitamin has been observed. Investigators[1] from the E. L. Patch Company Laboratories in Boston have reported a somewhat different interrelationship, relief of one vitamin deficiency with a different accessory food factor.

Vitamin E is usually called the fertility vitamin. In its absence, both male and female rats are sterile. The fertilized ovum attaches to the uterus, but is subsequently resorbed. For a long time it was believed that the sole function of vitamin E was to permit reproduction, that the normal individual did not require it for maintenance. More recently it has been shown that prolonged absence of E from the ration causes a muscular dystrophy and paralysis. Its deficiency has pronounced effects upon all the endocrine glands. According to Biddulph and Meyer,[2] of the University of Wisconsin, it causes a decrease in weight of the rat testes to one-half normal, with no discernible effect upon the weight or function of the ovary. It causes an increase in weight of male adrenals and an increase of 100 per cent in male thyroids, but no enlargement of either female thyroids or adrenals. There are other changes in the endocrine chain in E deficiency.

Holmes and Pigott[1] administered to young E-deficient rats with various degrees of muscular

1. Holmes, A. D.; and Pigott, M. G.: The Effect of Thiamin Hydrochloride on the Muscular Dystrophy of Avitaminosis-E. Amer. Jour. Physiol., **158**:211 (Feb.) 1941.

2. Biddulph, C.; and Meyer, R. K.: The Influence of Vitamin E Deficiency on the Endocrine Glands of Rats, Particularly on the Gonadotropic Hormone Content of the Pituitary Gland. Amer. Jour. Physiol., **132**:259 (Feb.) 1941.

impairment a ration high in vitamin B_1; and they report that the animals were restored to normal and developed with apparent normality to full maturity. Another group of E-deficient animals was given large doses of pure thiamin, B_1, by mouth, and also recovered from the symptoms of E deficiency in a few days. All the thiamin treated E-deficient rats developed normally and remained in good health. Massive doses of thiamin were used, from 4 to 14 international units per rat.

Vitamin E and thiamin seem chemically unrelated. They are not even in the same large grouping, since the first is fat-soluble and the second belongs to the water-soluble B group. It is of interest that deficiency symptoms of the one, E deficiency, were relieved by administration of large quantities of the other vitamin, B_1. The mechanism is difficult to explain.

It is also of interest that testicular atrophy and muscular dystrophy both follow E deficiency and that E deficiency may be a cause of thyroid enlargement. The relationship of the gonads to muscle function has not been studied. Since muscular development is a secondary sex characteristic, one might expect some parallelism with gonadal activity.

TWENTY-FIVE YEARS AGO

From Journals of 1916

English Dentists.[1]—The institution of a diploma in dental surgery took place comparatively recently in this country * * * the number of qualified dentists is far short of the requirements of the population, and a large number of unqualified men practice. They are not prevented from doing this, but they must not call themselves dentists. This is a very small drawback as they can exhibit sets of teeth and call themselves "tooth specialists." * * * No appreciable increase in the members of the dental profession can be looked for until the law gives further protection to the qualified man versus the unqualified.

Measles in the English Army.[2]—During the present year there has been a large increase in the mortality from measles. * * * Measles has caused a large amount of disablement among the troops.

Pineal Gland.[3]—That minute particle of tissue, no larger than a pea, known as the epiphysis cerebri, or pineal gland, has long been an object of curiosity to students of anatomy and physiology * * * speculations concerning its functions have ranged from considering it as the source of a secretion controlling anatomical development to an idea that it is the center of intelligence or the seat of the soul. * * * Dr. W. E. Dandy * * * has succeeded in removing the pineal glands from a number of puppies without apparently influencing their growth or development in any respect. They are neither larger nor smaller, fatter nor leaner, brighter nor more stupid than their controls, and their sexual development was neither precocious nor retarded.

The pineal gland would seem to be a structure residual and degenerate from a long vanished form of existence, a sort of appendix coniform, so to speak. * * * to use it or extracts made from it as a therapeutic agent is absurd.

National Defense.[4]—Preparedness for national defense is the most absorbing topic of the day. In every newspaper and magazine we see discussed various plans for increasing the Army and Navy and otherwise strengthening our national defense. * * * Little, however, has reached the lay press regarding the most important phase of the preparedness question, i. e., the provisions for protecting the citizens of the United States who may enter the Army as regulars, or as national guardsmen, against the diseases which have killed more soldiers than the shot and shell of their enemies. * * *

The Spanish-American War * * * developed the greatest sanitarian in the history of the world * * * Gorgas. * * *

It is most fortunate at this time, when military preparedness is being considered, that the greatest sanitary genius of the age is Surgeon-General of the United States Army.

Wassermann Reaction.[5]—The Wassermann reaction, one of our most valuable methods of establishing the existence or non-existence of syphilis in an individual under observation, has recently been criticized very severely by several members of the medical profession.

Uhle and Mackinney, in a series of 107 tests on patients clinically free of syphilis, and with no history of syphilis, obtained a positive Wassermann reaction in from 2.6 to 18.1 per cent of the cases examined. This work was done by ten different serologists.

In patients suffering with primary, secondary and tertiary syphilis in a series of several hundred cases, the positive results varied from 50 to 100 per cent; and in a series of 168 cases five different serologists agreed in their findings in but 47 per cent of the cases.

1. London Letter. J.A.M.A., **66**:46, 1916.
2. Ibid,, p. 47.
3. Editorial. The Pineal Gland Inert. Sou. Med. Jour., **9**: 290, 1916.
4. Ibid., p. 274.
5. Shropshire, Courtney W.; and Watterston, Chas.: A Plea for Uniformity in the Wassermann Reaction. Ibid., p. 205.

Book Reviews

Electrocardiography in Practice. By Ashton Graybiel, M.D., Assistant in Medicine, Massachusetts General Hospital, and Paul D. White, M.D., Lecturer in Medicine, Harvard Medical School; Physician, Massachusetts General Hospital, in Charge of the Cardiac Clinics and Laboratory. Philadelphia: W. B. Saunders Company, 1941. 317 pages, illustrated. Cloth $6.00.

This book is written to show the uses and limitations of electrocardiography. The first section is devoted to electrocardiograms illustrating the normal heart,

forms of arrhythmia and patterns associated with different cardiac abnormalities. There is a brief summary of the subjective and objective symptoms found in each case and these are correlated with the findings in the graph. In some of the graphs the ordinates are spaced at one-fifth of a second, which makes their analysis more difficult. The interpretations of the graphs are well presented and have not been too technically given, so that the general practitioner should be able to analyze them. A clear picture is given of the deviations of the graph in congenital heart disease and infections, as well as in avitaminosis, endocrine disease and some drug reactions except that opium is omitted, which is to be regretted, since frequently it is used as a therapeutic agent in heart disease. The section devoted to artefacts gives many practical points in their recognition. The sections allotted to hypertensive heart disease and acute and chronic "cor pulmonale" are brief but complete. Coronary heart disease, as presented in this book, is one of the outstanding features; for the data upon which a diagnosis can be made from the graph alone, the atypical graph, and substantiation of other data, are examples of perfect clarity. The second section, "Electrocardiograms for Practice and Interpretation," shows a good selection of graphs; but the longer distance between the ordinates (one-fifth second) is a liability. The appendix is devoted to an analytical electrocardiographic index which gives the normal dimensions of the components of the electrocardiographic registrations.

The Head and Neck in Roentgen Diagnosis. By Henry K. Pancoast, M.D., Late Professor of Radiology and Director of the Department of Radiology, University of Pennsylvania; Eugene P. Pendergrass, M.D., Professor of Radiology and Director of the Department of Radiology, University of Pennsylvania; J. Parsons Schaeffer, M.D., Ph.D., Professor of Anatomy and Director of the Daniel Baugh Institute of Anatomy, Jefferson Medical College. 976 pages, illustrated. Springfield, Illinois: Charles C. Thomas, 1940. Cloth $12.50.

This book, "The Head and Neck in Roentgen Diagnosis," is richly illustrated and covers 976 pages. At the end of each chapter there is a very complete bibliography, and at the end of the book an index referring to text pages as well as pages upon which figures appear. The roentgenologic appearance of the normal head and neck is discussed; also the anomalies, diseases and injuries of these structures. In the general outline of the book an important feature is the full discussion of the anatomy by Dr. Schaeffer. Chapters IX and X on intracranial tumors and cerebral pneumography, respectively, are excellent; they include not only the writer's opinion, but those of various other authorities. The clinical symptoms are correlated with the roentgenologic findings, making it much more valuable to the radiologist than merely describing the radiologic appearance. There is a great deal of space devoted to the soft tissues of the neck, which is well justified by the strong current interest in this subject.

This book is noteworthy for its completeness, clarity and abundance of accurate information. It is difficult to describe in a short review and cannot be recommended too highly, particularly to radiologists who are interested in the correlation of technical procedure with medical diagnosis.

Radiologic Physics. By Charles Weyl, S. Reid Warren, Jr., Dallett B. O'Neill, Moore School X-Ray Laboratory, Moore School of Electrical Engineering, University of Pennsylvania. With a Foreword by Eugene P. Pendergrass, M.D., Director of the Department of Radiology, University of Pennsylvania. 459 pages, illustrated. Springfield, Illinois: Charles C. Thomas, 1941. Cloth $5.50.

This material is wide in scope, adequate in detail, and the method of presentation seems excellent. A comprehensive bibliography, together with appendices (physical and mathematical reviews, log tables, etc.) adds much to the value of the work. As one of the best of the too few texts in this field, it fills a definite need, both in teaching and in research. The elementary form of introduction is advantageous to those of inadequate mathematical background, while the more advanced sections are comprehensive enough to cover the needs of the graduate radiologist. It should be included in medical libraries.

Cyclopropane Anesthesia. By Benjamin Howard Robbins, B.A., M.S., M.D., Associate Professor of Pharmacology, Vanderbilt University School of Medicine. 154 pages, illustrated. Baltimore: The Williams & Wilkins Company, 1940. Cloth $3.00.

This book consists of a review of the experimental and clinical investigations on cyclopropane with indications and contraindications for its use. The author evaluates the existing knowledge of over 200 published papers with practical experiences in some 250,000 clinical anesthesias. It is an invaluable asset to the individual interested in the progress of anesthesia.

Argyria: The Pharmacology of Silver. By William R. Hill, M.D., Instructor in Dermatology and Syphilology, University of Pennsylvania, and Donald M. Pillsbury, M.A., M.D., Associate Professor of Dermatology and Syphilology, University of Pennsylvania. 133 pages. Baltimore: The Williams & Wilkins Company, 1939. Cloth $2.50.

For a long time it was a mild reproach of American medical literature that few monographs appeared. Recent years are seeing a change for the better in this regard; and the small volume under discussion in this review is a fine example of a good monograph.

The arrangement is admirable; the lay reader by reading the summaries at the end of each chapter and chapter five itself, may within a half hour find out all there is at present known about argyria; the research worker or the student requiring knowledge of sources and technical details will find his needs filled by the thorough treatment of the subject matter appearing in the book as a whole.

Every close observer in the profession is aware, as the authors point out, that argyria is on the increase; hundreds of mild cases resulting from overuse of "argyrol," "neo-silvol" and other silver preparations are never reported, and often not recognized by the family physician; the incidence as reflected in the literature is no indication of the importance of the subject. The physician who wishes to acquaint himself fully with the effects of silver medication will find what he seeks in this volume.

The 1940 Year Book of Pathology and Immunology. Edited by Howard T. Karsner, M.D., Professor of Pathology, Director of the Institute of Pathology, Western Reserve University, Cleveland, and Sanford B. Hooker, A.M., M.D., Professor of Immunology, Boston University School of Medicine; Immunologist, Massachusetts Memorial Hospitals. 688 pages, illustrated. Chicago: The Year Book Publishers, 1940. Cloth $3.00.

The value of the Year Book publications is well established and the addition of a Year Book of Pathology and Immunology will be welcomed by all those who have felt the need of such a volume. The range of pathology is so great that it includes the whole of medicine. An annual review of its advances is of value not only to the pathologist, but also to those in other branches of medicine. The book follows the general plan of previously published year books. The opening section deals with general pathology. It is followed by a section on the pathology of tumors and a section on each of the systems. The concluding sections cover immunology and technic. Where recent articles have been found to represent only fragments in a series of consecutive studies, at the invitation of the author, some of the investigators have prepared summaries of their research. The only criticism applicable is that the size of the volume does not allow review of all the publications of importance.

Southern Medical News

DALLAS SOUTHERN CLINICAL SOCIETY

The Thirteenth Annual Spring Clinical Conference of the Dallas Southern Clinical Society will be held at the Adolphus Hotel, Dallas, Texas, March 17-20. In addition to the twelve honor guest speakers there will be clinical presentation by a group of local physicians. The entertainment features a smoker on Monday evening and the annual banquet on Thursday evening. A registration fee of $10.00 covers all features—the scientific activities, the round-table luncheons, the smoker and the banquet. Officers of the Society are: Dr. Everett C. Cox, President; Dr. Howard K. Crutcher, Vice-President; Dr. Charles H. Warren, 1133 Medical Arts Building, Secretary; Dr. Tom H. Cheavens, Treasurer; Dr. W. Grady Reddick, Chairman of Executive Committee; and Dr. Ozro T. Woods, Chairman of Program Committee.

MISSISSIPPI VALLEY MEDICAL SOCIETY

The Mississippi Valley Medical Society offers annually a cash prize of $100.00, a gold medal, and a certificate of award for the best unpublished essay on any subject of general interest (including medical economics) and practical value to the general practitioner of medicine. Certificates of merit may also be granted to physicians whose essays are rated second and third best. For details write Dr. Harold Swanberg, Secretary, 209-224 W.C.U. Building, Quincy, Illinois.

ALABAMA

Dr. Rutherford O. Ingham, Livingston, formerly Health Officer of Bibb County, has been assigned to a similar position in Limestone County.

Dr. Robert W. Todd, formerly of New Orleans, Louisiana, has been appointed Health Officer of Russell County, succeeding Dr. Marion L. Shaddix, Phenix City, who recently was transferred to Clay County.

Dr. Ralph H. Allen, formerly of Ruston, Louisiana, has been placed in charge of the health activities in Henry County.

DEATHS

Dr. Warren Sutton Baldwin, Verbena, aged 68, died January 29.

Dr. Edgeworth Stephens Casey, Birmingham, aged 63, died November 12 of duodenal ulcer and nephritis.

Dr. William George Carnathan, Butler, aged 58, died November 30 of intestinal obstruction.

Dr. Henry Claiborne McCullough, Town Creek, aged 73, died November 8 of carcinoma of the parotid gland.

Dr. James J. Strickland, Birmingham, aged 61, died recently.

Dr. John Yeilding, Hanceville, aged 78, died November 12 of acute dilatation of the heart, chronic myocarditis and nephritis.

ARKANSAS

Boone County Medical Society has elected Dr. Ulys Jackson, President; Dr. W. H. Poynor, Vice-President; and Dr. J. G. Gladden, Secretary-Treasurer, all of Harrison.

Searcy County Medical Society has elected Dr. E. W. Wood, President; Dr. J. O. Leslie, Vice-President; and Dr. Sam G. Daniel, Secretary-Treasurer, all of Marshall.

Chicot County Medical Society has elected Dr. W. J. Hutson, Eudora, President; Dr. C. G. Leverett, Eudora, Vice-President; and Dr. W. J. Schwarz, Lake Village, Secretary-Treasurer.

Conway County Medical Society has elected Dr. J. F. Halbrook, Plumerville, President; Dr. C. E. Etheridge, Morrilton, Vice-President; and Dr. C. Ray Williams, Morrilton, Secretary-Treasurer.

Desha County Medical Society has elected Dr. C. H. Kimbro, Tillar, President, and Dr. Gibbs Biscoe, Dumas, Secretary-Treasurer.

Fifth Councilor District Medical Society has elected Dr. John H. Wilson, Magnolia, President; Dr. A. D. Cathey, El Dorado, Vice-President; and Dr. Rowland B. Robins, Camden, Secretary.

Lincoln County Medical Society has elected Dr. C. W. Dixon, Gould, President; Dr. G. W. Ringgold, Gould, Vice-President; and Dr. L. T. Taylor, Star City, Secretary-Treasurer.

Miller County Medical Society has elected Dr. L. H. Lanier, President; Dr. W. D. Smith, Vice-President; and Dr. J. W. Burnett, Secretary-Treasurer, all of Texarkana.

Phillips County Medical Society has elected Dr. Edward Kultgen, Elaine, President; Dr. W. B. Connolly, Helena, Vice-President; and Dr. H. H. Rightor, Helena, Secretary-Treasurer.

Washington County Medical Society has elected Dr. R. H. Huntington, President; Dr. H. H. Howze, Vice-President; and Dr. V. O. Lesh, Secretary-Treasurer, all of Fayetteville.

Medical Arts Club of Little Rock has elected Dr. Carl A. Rosenbaum, President; Dr. R. E. McLochlin, Vice-President; Dr. W. Myers Smith, Secretary; Dr. Wilfred Parsons, Treasurer; and Dr. Howard Stern, Corresponding Secretary.

Dr. E. J. Stroud has been elected a Director of the Jonesboro Chamber of Commerce.

Dr. L. S. Dunaway has been appointed physician to the Arkansas State Teachers College, Conway, during the absence of Dr. Hugh C. Brooke on military duty.

Dr. Van C. Binns, Pine Bluff, has been called for military service with the U. S. Army and is stationed at Fort Bliss, Texas, with the rank of Captain.

Dr. A. F. Hoge has been elected a Director of the City National Bank at Fort Smith.

Dr. Joseph F. Malloy, formerly of Omaha, is associated with Dr. F. A. Gray, Batesville.

Dr. W. J. Ketz is now associated with Dr. O. J. T. Johnston at Batesville.

Dr. W. B. Grayson, Dr. L. R. Hodges and Dr. W. G. Hodges, Malvern, have been appointed to the State Board of Embalmers.

Reserve Medical Officers ordered to active duty at the Medical Field Service School, Carlisle Barracks, Pennsylvania, are: Capt. O. G. Hirst, Prescott; Lt. T. L. Adais, Bald Knob; Lt. B. P. Briggs, Little Rock; Lt. H. D. Fowler, Little Rock; Lt. E. J. Ritchie, North Little Rock; Lt. T. S. Van Duyn, Stuttgart.

The following have been called to active duty with the 153rd Infantry, Arkansas National Guard, at Camp Robinson: Lt. Col. Howell Brewer, Hot Springs; Major H. C. Brooke, Conway; Lt. C. A. Archer, Jr., DeQueen; Lt. C. L. Hyatt, Little Rock.

Dr. C. S. Paddock, formerly of Memphis, Tennessee, is now located at Fayetteville.

Dr. L. E. Ellison, formerly of St. Louis, Missouri, has moved to Warren.

Dr. J. F. John has been elected a Director of the Bank of Eureka Springs.

Dr. F. C. Maguire has been transferred from Monroe County to Mississippi County as Health Director.

Dr. O. R. Keely has been elected a Director of the Grant County Bank at Sheridan.

Dr. C. P. Cisco has been elected a Director of the First State Bank at Springdale.

Dr. D. L. Owens has been elected a Director of the Harrison County Club.

Dr. H. E. Mobley is a Director of the Federal Savings and Loan Association of Morrilton.

Dr. D. E. White is President of the El Dorado Library Board.

DISTRICT OF COLUMBIA

A special practical course in ocular surgery, pathology and orthoptics will be presented in Washington on April 14-18 by the resident staffs of the George Washington University School of Medicine and the Army Medical Museum. Additional information may be obtained from the Secretary, 927 Seventeenth Street, N.W., Washington.

Rear Admiral P. S. Rossiter, M.C., U. S. Navy, Retired, Washington, Chairman of the Committee on Medical Aid of the 1941 Inaugural Committee, appointed the following members of the Society to assist him in making plans for providing medical care on Inauguration Day, January 20: Dr. William A. Morgan, Vice-Chairman; Dr. Walter A. Bloedorn, Dr. Daniel L. Borden, Dr. James A. Cahill, Jr., Dr. George W. Calver, Dr. Worth B. Daniels, Dr. William Thornwall Davis, Dr. William P. Herbst, Dr. Howard F. Kane, Dr. A. Magruder MacDonald, Dr. F. X. McGovern, Dr. William Gerry Morgan, Dr. Ivy A. Pelzman, Dr. Charles Stanley White, Dr. Eugene R. Whitmore and Dr. William M. Yater.

Providence Hospital was presented with a $1,600 mechanical respirator on December 3 by Past District Department American Legion Commander William T. Slattery. The necessary funds to purchase this respirator were raised by thirty-nine American Legion Posts and their Auxiliaries.

The new Southwest Health Center, Washington, a three-story building, erected at a cost of $200,000, was dedicated and opened for inspection December 18 by the District Health Department. Dr. Charles B. Campbell delivered the invocation and Dr. George C. Ruhland was presented a certificate of merit by the Southwest Citizens' Association.

Dr. Arthur C. Christie, Washington, has resigned as Chairman of the Public Health Commission of the Washington Board of Trade and will be succeeded by Dr. Roy Lyman Sexton.

Dr. Custis Lee Hall, Washington, received a silver tray and candelabra from the Kiwanis Club December 15 in recognition of his sixteen years' service in treating crippled children in the Kiwanis Club.

Seventeen barracks will be built to house enlisted personnel ordered to the Walter Reed General Hospital, Washington, for technical training as laboratory, roentgen ray and dental technicians, ward masters and ward nurses and in other capacities.

Deaths

Dr. Gist Blair, Washington, aged 81, died December 16.

Dr. Carl Roger Darnall, Washington, aged 73, died January 18 of arteriosclerosis.

Dr. Charles Wardell Stiles, Washington, aged 74, died January 24 at Winter Park, Florida.

FLORIDA

The South Atlantic Association of Obstetricians and Gynecologists held its annual meeting at Jacksonville, February 7-8.

Dade County Medical Society has elected Dr. C. Larimore Perry, President; Dr. T. O. Otto, Vice-President; Dr. Herbert Eichert, Secretary; and Dr. W. L. Fitzgerald, Treasurer.

Duval County Medical Society has installed Dr. S. R. Norris, President, and elected Dr. Ernest B. Milam, President-Elect; Dr. James M. Bryant, Vice-President; Dr. F. Gordon King, Secretary; and Dr. Alan Brown, Treasurer, all of Jacksonville.

Hillsborough County Medical Society has elected Dr. Robert G. Nelson, President; Dr. B. W. Lowry, Vice-President; and Dr. J. S. Grable, Secretary-Treasurer, all of Tampa.

Lake County Medical Society has elected Dr. Marion B. O'Kelley, Leesburg, President; Dr. Louis R. Bowen, Eustis, Vice-President; and Dr. Clyde Bowie, Leesburg, Secretary-Treasurer.

Lee County Medical Society has elected Dr. M. F. Johnson, President; Dr. A. S. Byle, Vice-President; and Dr. H. Quillian Jones, Secretary-Treasurer, all of Fort Myers.

Orange County Medical Society has elected Dr. Frank D. Gray, Orlando, President; Dr. Spencer Folsom, Orlando, President-Elect; Dr. J. F. Gardner, Winter Park, Vice-President; Dr. Fred Mathers, Orlando, Secretary; and Dr. H. C. Ingram, Orlando, Treasurer.

Palm Beach County Medical Society has elected Dr. W. O. Arnold, President; Dr. J. R. Sory, Vice-President; Dr. Victor Clarholm, Secretary; and Dr. F. K. Herpel, Treasurer, all of West Palm Beach.

Pasco-Hernando-Citrus County Medical Society has elected Dr. W. B. Moon, Crystal River, President; Dr. W. W. Jones, Dade City, First Vice-President; Dr. S. C. Harvard, Brooksville, Second Vice-President; Dr. G. R. Creekmore, Brooksville, Secretary-Treasurer, reelected.

Polk County Medical Society has elected Dr. Bruce R. Tinkler, Lake Wales, President; Dr. L. L. Lancaster, Bartow, Vice-President; and Dr. Edgar Watson, Lakeland, Secretary-Treasurer.

Seminole County Medical Society has elected Dr. K. R. Bell, President; Dr. G. S. Selman, Vice-President; and Dr. T. F. McDaniel, Secretary-Treasurer, all of Sanford.

Volusia County Medical Society has elected Dr. J. R. Chandler, Daytona Beach, President; Dr. W. C. Pay, DeLand, Vice-President; and Dr. R. L. Miller, Daytona Beach, Secretary-Treasurer.

Walton-Okaloosa County Medical Society has elected Dr. A. G. Williams, Lakewood, President; and Dr. R. B. Spires, DeFuniak Springs, Secretary.

Dr. O. O. Feaster, St. Petersburg, was elected First Vice-President of the Radiological Society of North America at its meeting held in Cleveland, Ohio, December 2-6.

Dr. Shaler Richardson, Jacksonville, has been elected President of the State Board of Health, succeeding the late Dr. N. A. Baltzell. Dr. Courtland D. Whitaker, Mariana, has been selected to succeed Dr. Baltzell as physician to the Florida Industrial School for Boys in that city.

Dr. Joseph Jordan Eller, formerly of New York City, announces the opening of offices in the Harvey Building, West Palm Beach, for the practice of diseases of the skin, x-ray and radium therapy.

Dr. Leo M. Wachtel and Miss Helen Ross Dixon, both of Jacksonville, were married January 7.

Dr. S. Roy Higginbotham, Jr., Tampa, and Miss Esther E. Burnes, Atlanta, were married September 4.

Deaths

Dr. Charles Merritt Ausley, Tallahassee, aged 61, died November 22 of bronchopneumonia and arthritis.

Dr. Van William Burns, Stuart, aged 39, died December 23.

Dr. Caroline Herring Dennis, St. Petersburg, aged 77, died November 25 of carcinoma of the rectum.

Dr. William H. Martin, Winter Haven, aged 78, died November 19.

Dr. Samuel Miles Robinson, Orlando, aged 84, died December 4 of typhus fever, chronic myocarditis and arteriosclerosis.

GEORGIA

Medical Association of Georgia will hold its ninety-second annual session at Macon, May 13-16.

Bartow County Medical Society has elected Dr. W. B. Quillian, President; Dr. Tanner Lowry, Vice-President; and Dr. A. L. Horton, Secretary-Treasurer, all of Cartersville.

Brooks County Medical Society has elected Dr. M. E. Groover, President; Dr. J. R. McMichael, Vice-President; and Dr. Harry A. Wasden, Secretary-Treasurer, all of Quitman.

Bulloch-Candler-Evans Counties Medical Society has elected Dr. A. B. Daniels, Statesboro, President; Dr. R. L. Kennedy, Metter, Vice-President; and Dr. L. H. Griffin, Claxton, Secretary-Treasurer.

Carroll County Medical Society has elected Dr. B. C. Powell, Villa Rica, President, and Dr. D. S. Reese, Carrollton, Secretary-Treasurer.

Cherokee-Pickens Counties Medical Society has elected Dr. Jno. P. Turk, Nelson, President; Dr. M. G. Hendrix, Ball Ground, Vice-President; and Dr. Robert T. Jones, Canton, Secretary-Treasurer.

Cobb County Medical Society has elected Dr. M. M. Hagood, Marietta, President; Dr. F. P. Lindley, Powder Springs, Vice-President; and Dr. W. C. Mitchell, Smyrna, Secretary-Treasurer.

Chattooga County Medical Society has elected Dr. R. E. Talley, President; Dr. Mary M. McLeod, Vice-President; and Dr. W. B. Mitchell, Secretary-Treasurer, all of Trion.

Dooly County Medical Society has elected Dr. L. H. Bishop, Unadilla, President, and Dr. M. L. Malloy, Vienna, Secretary-Treasurer.

Douglas County Medical Society has elected Dr. R. E. Hamilton, President; Dr. C. V. Vansant, Vice-President; and Dr. T. B. Taylor, Secretary-Treasurer, all of Douglasville.

Dougherty County Medical Society has elected Dr. R. D. McKenzie, President; Dr. W. M. Feild, Vice-President; and Dr. I. M. Lucas, Secretary-Treasurer, all of Albany.

Floyd County Medical Society has installed Dr. W. A. Sewell, President; and has elected Dr. Lester Harbin, President-Elect; and Dr. Warren M. Gilbert, Secretary-Treasurer, all of Rome.

Fulton County Medical Society has installed Dr. Howard Hailey, President; and elected Dr. Major F. Fowler, President-Elect; Dr.

Continued on page 36

Laxatives

not needed to relieve

Constipation

when the daily feedings are prepared from milk properly modified with

Mellin's Food

Samples sent to physicians upon request.

Constipation in Infancy

Constipation in infancy probably commands the physician's attention more often than any other symptom that points to the need of readjusting a feeding formula.

Constipation is a common complaint and oftentimes is the real reason for a slow gain in weight, restless nights and a fretful, uncomfortable baby.

Infants fed on milk and water in proportions suitable for healthy babies of given age and weight with an amount of Mellin's Food to meet the carbohydrate requirement (*six to eight level tablespoons to the full day's mixture*) are seldom constipated.

Many physicians use Mellin's Food routinely in preparing bottle feedings, for they know from experience that regular stools of good consistency are characteristic of babies fed on milk properly modified with Mellin's Food. These physicians thus avoid much of the trouble associated with infant feeding.

Mellin's Food Co., Boston, Mass.

MELLIN'S FOOD: Produced by an infusion of Wheat Flour, Wheat Bran and Malted Barley admixed with Potassium Bicarbonate—consisting essentially of Maltose, Dextrins, Proteins and Mineral Salts.

Continued from page 342

Stephen T. Barnett, Jr., Vice-President; and Dr. J. G. McDaniel, Secretary-Treasurer, all of Atlanta.

Georgia Medical Society has installed Dr. H. H. McGee, President, and elected Dr. E. N. Gleaton, President-Elect; Dr. W. E. Brown, Vice-President; Dr. S. Elliott Wilson, Secretary-Treasurer, all of Savannah.

Glynn County Medical Society has elected Dr. M. E. Winchester, President; Dr. Webb Conn, Vice-President; and Dr. T. V. Willis, Secretary-Treasurer, all of Brunswick.

Meriwether County Medical Society has elected Dr. J. A. Johnson, Manchester, President; Dr. W. K. Kirkland, Manchester, Vice-President; and Dr. R. B. Gilbert, Greenville, Secretary-Treasurer.

Muscogee County Medical Society has elected Dr. W. Edward Storey, President; Dr. Arthur N. Berry, Vice-President; and Dr. Roy L. Gibson, Secretary-Treasurer, all of Columbus.

McDuffie County Medical Society has elected Dr. B. F. Riley, President, and Dr. C. W. Churchill, Secretary-Treasurer, both of Thomson.

Polk County Medical Society has elected Dr. Geo. M. White, Rockmart, President; Dr. C. V. Wood, Cedartown, Vice-President; and Dr. John M. McGehee, Cedartown, Secretary-Treasurer.

Randolph County Medical Society has elected Dr. Loren Gary, Georgetown, President; Dr. F. M. Martin, Shellman, Vice-President; and Dr. W. G. Elliott, Cuthbert, Secretary-Treasurer.

Tattnall County Medical Society has elected Dr. C. B. Walling, Collins, President; Dr. G. W. Tootle, Glennville, Vice-President; and Dr. J. M. Hughes, Glennville, Secretary-Treasurer.

Telfair County Medical Society has elected Dr. John T. Persall, Jr., McRae, President, and Dr. F. P. Hardin, Lumber City, Secretary-Treasurer.

Terrell County Medical Society has elected Dr. Guy Chappel, Dawson, President; Dr. J. T. Arnold, Parrott, Vice-President; and Dr. J. C. Tidmore, Dawson, Secretary-Treasurer.

Tift County Medical Society has elected Dr. T. F. Little, President; Dr. C. S. Pittman, Vice-President; and Dr. R. E. Jones, Secretary-Treasurer, all of Tifton.

Turner County Medical Society has elected Dr. H. M. Belflower, Sycamore, President; Dr. W. L. Story, Ashburn, Vice-President; and Dr. J. H. Baxter, Ashburn, Secretary-Treasurer.

Georgia Pediatric Society has installed Dr. R. C. McGahee, Augusta, President; Dr. E. N. Gleaton, Savannah, President-Elect; Dr. J. Harry Lange, Atlanta, Vice-President; and Dr. Don F. Cathcart, Atlanta, Secretary-Treasurer.

Piedmont Hospital, Atlanta, has elected on its staff Dr. Carter Smith, President; Dr. Wm. H. Trimble, Vice-President; and Dr. T. Sterling Claiborne, Secretary.

St. Joseph's Hospital, Savannah, has elected on its staff Dr. J. Reid Broderick, President; Dr. J. E. Porter, Vice-President; and Dr. D. J. McCarthy, Secretary-Treasurer.

Officers of the Medical Staff of Emory University Hospital, Atlanta, are: Dr. M. K. Bailey, President; Dr. A. V. Hallum, Vice-President; and Dr. Chas. A. Everhart, Secretary.

Emory University School of Medicine, Atlanta, has received $100,000 from the Joseph B. Whitehead Foundation for the purpose of endowing further the Joseph B. Whitehead chair in surgery. An additional $16,500 was given the medical school for use in connection with the chair in memory of Conkey P. Whitehead, who died in November. The Foundation was first established after the death of Joseph B. Whitehead, Jr., who willed his estate as a memorial to his father for the support of philanthropic and educational enterprises in the Atlanta area. The professorship was created in 1939 by the Foundation gift of $250,000.

Dr. J. K. Hall, Lyons, has been appointed on the staff of Governor Eugene Talmadge with the rank of Lieutenant Colonel.

Dr. M. B. Copeloff, Atlanta, has been appointed a member of the State Board of Medical Examiners for a four-year term.

Dr. Lon Grove announces the association of Dr. Fred F. Rudder in the practice of surgery with offices in the Medical Arts Building, Atlanta.

Dr. H. B. Bradford has moved from Pine Log to Cartersville and will have offices in the Howell-Quillian Clinic.

Dr. M. A. Fort, Bainbridge, has been elected President of the Southwestern Section of the Georgia Public Health Association.

Dr. G. K. Cornwell has moved from Milledgeville to Eastman and joined the staff of the Eastman Clinic.

Dr. Lewis Howard McDonald and Miss Lois Reeve, both of Atlanta, were married October 12.

Continued on page 38

ST. LOUIS CLINICS

ANNUAL

CLINICAL CONFERENCE

March 10-13, 1941

Place of Meeting—Coronado Hotel

The St. Louis Clinics will offer an intensive course in various branches of medicine, surgery and surgical specialties. The Conference will be given by members of the medical profession of St. Louis; outstanding medical officers of the Army and Navy, and the following guest clinicians:

FRED L. ADAIR, M.D., Professor of Obstetrics and Gynecology, The University of Chicago School of Medicine, Chicago.

WILLIAM L. BRADFORD, M.D., Associate Professor of Pediatrics, University of Rochester Medical School, Rochester.

CHARLES A. DOAN, M.D., Professor of Medicine, The Ohio State University, Columbus.

WILLIS D. GATCH, M.D., Dean and Professor of Surgery, Indiana University School of Medicine, Indianapolis.

JOHN J. SHEA, M.D., Member, American Laryngological, Rhinological and Otological Society, Memphis.

ARTHUR STEINDLER, M.D., Professor of Orthopedic Surgery, The State University of Iowa, Iowa City.

FRED D. WEIDMAN, M.D., Professor of Dermatologic Research and Vice-Dean for Dermatology-Syphilology, Graduate School of Medicine, University of Pennsylvania, Philadelphia.

Daily Programs from Nine to Five—Three Round Table Luncheon Discussions
Two Evening Programs

The registration fee of ten dollars includes the round table luncheons.

FOR INFORMATION ADDRESS THE ST. LOUIS CLINICS

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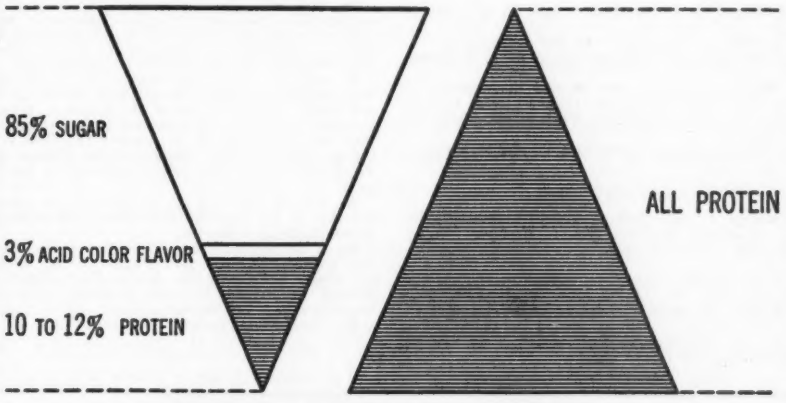

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Continued from page 36

Dr. Richard F. Slaughter, Augusta, and Miss Jane Carruthers, Winder, were married October 10.

Dr. Frank Matthews Parish, Brunswick, and Miss Martha Elizabeth Mobley, both of Atlanta, were married in October.

Dr. Arthur Park McGinty, Atlanta, and Miss Murray Smith, Birmingham, Alabama, were married recently.

Deaths

Dr. Horace E. Evans, Perry, aged 56, died December 14 when a train struck his automobile.

Dr. Luke Irdel Foster, Ellijay, aged 33, died December 10 of heart disease.

Dr. Virgil Eugene Franklin, Graymont, aged 70, died November 13 of cerebral hemorrhage.

Dr. Charles Floyd Griffith, Griffin, aged 56, died January 1.

Dr. Thomas Hightower Hancock, Atlanta, aged 71, died November 17.

Dr. Thomas Lamar Harris, Wrightsville, aged 78, died December 13.

Dr. Delon L. Murray, Dexter, aged 60, died December 11.

Dr. William Thomas Spears, Rutledge, aged 83, died December 7.

Dr. W. A. Walden, Davisboro, aged 70, died November 20.

Dr. William Van Vorst Parramore, Cochran, aged 56, was killed November 27 when the automobile which he was driving was struck by a train.

Dr. Charles Jefferson Woods, Macon, aged 60, died November 6.

KENTUCKY

Bracken-Pendleton County Medical Society has elected Dr. C. F. Haley, Brooksville, President; Dr. J. M. Blades, Butler, Vice-President; and Dr. W. A. McKenney, Falmouth, Secretary-Treasurer.

Calloway County Medical Society has elected Dr. W. H. Mason, Murray, President; Dr. C. H. Jones, Lynn Grove, Vice-President; and Dr. J. A. Outland, Murray, Secretary-Treasurer.

Franklin County Medical Society has elected Dr. Grace Snyder, President; Dr. L. L. Cull, Vice-President; and Dr. T. P. Leonard, Secretary-Treasurer, all of Frankfort.

Daviess County Medical Society has elected Dr. E. Dargan Smith, President; Dr. W. B. Negley, Vice-President; and Dr. Thomas H. Milton, Secretary-Treasurer, all of Owensboro.

Harrison County Medical Society has elected Dr. M. J. McNeely, Berry, President; Dr. R. L. Loftin, Pikeville, Vice-President; and Dr. W. B. Moore, Cynthiana, Secretary-Treasurer.

Johnson County Medical Society has elected Dr. J. A. Wells, President; Dr. W. E. Akin, Vice-President; and Dr. A. D. Slone, Secretary-Treasurer, all of Paintville.

Madison County Medical Society has elected Dr. Wilson F. Dodd, Berea, President; Dr. Harvey C. Blanton, Richmond, Vice-President; and Dr. Robert L. Rice, Richmond, Secretary-Treasurer.

Whitley County Medical Society has elected Dr. H. W. Terrell, Corbin, President; Dr. Raymond Ohler, Corbin, Vice-President; and Dr. C. A. Moss, Williamsburg, Secretary-Treasurer.

The Association of Surgeons of the Southern Railway System will hold their annual convention in the Brown Hotel, Louisville, May 25-27.

Dr. William J. Gerding, Newport, was honored with a testimonial dinner December 12 by his colleagues on the staff of St. Elizabeth's Hospital, Covington, on the completion of twenty-five years as instructor in materia medica in the school of nursing and thirty-two years on the staff of the hospital.

Dr. Addie M. Lyon, Superintendent of the Western State Hospital, Hopkinsville, has been appointed Director of state hospitals and mental hygiene to succeed Dr. Joseph G. Wilson, Frankfort, resigned. Dr. William R. Summers, Superintendent of the Central State Hospital, Lakeland, will succeed Dr. Lyon at Hopkinsville, and Dr. Isham Kimbell, Manager of the Veterans' Administration Facility at Gulfport, Mississippi, will come to the Lakeland Hospital.

Dr. John W. Fish and Dr. Samuel E. Parks announce their association in the practice of ophthalmology with offices in the Brown Building, Louisville.

Dr. B. M. Mummell, formerly of Fort Pierce, Florida, and who was graduated from Tufts Medical College, Boston, and was for several years with the Boston City Hospital, is now associated with Dr. M. M. Dunn, Richmond, with practice limited to eye, ear, nose and throat.

Dr. Louis Fine, formerly Director of the Hancock County

Continued on page 40

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Didactic lectures and active clinical application of all present-day methods of physical therapy in internal medicine, general and traumatic surgery, gynecology, urology, dermatology, neurology and pediatrics. Special demonstrations in minor electrosurgery, electrodiagnosis, fever therapy, hydrotherapy, including colonic therapy, light therapy.

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Autolyzing the yeast frees or develops a potent anti-anemic principle which has been identified as the extrinsic factor. There have been over sixty published reports in medical literature on the successful use of Vegex in the anemias.

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In their article on "Riboflavin Deficiency in Man" (*New England Journal of Medicine*, 221:921-926, 1939), Jolliffe, Fein and Rosenblum state that they found Vegex relieves both riboflavin deficiency and pellagra.

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Guest Speakers: Drs. Walter B. Lancaster, Hanover, N. H.; Louis H. Clerf, Philadelphia, Pa.; Frederick Davis, Madison, Wis.; LeRoy Schall, Boston, Mass.; Elbyrne G. Gill, Roanoke, Va.; Julius Lempert, New York City; Comdr. Julius Neuberger, U.S. Navy; also members of our own staff.

Address, Mabel R. Stewart, Registrar of the School, 218 Second Ave., New York City

Continued from page 38

Health Department at Hawesville, has been appointed to replace Dr. G. M. Wells as Director of the Warren County Health Department during the year that Dr. Wells will be in army service. Dr. Wells is Commander of the 149th Infantry Medical Department with the rank of Major.

Dr. N. C. Witt, Secretary of the Simpson County Medical Society for twenty-seven years, has resigned and Dr. R. Wilson has been elected as his successor.

Pineville Community Hospital, Pineville, has added a new addition, making it one of the most complete hospitals in the State.

Dr. Robert Cregor Bateman, Fort Knox, and Miss Charlotte Almada Wible, Lexington, were married December 19.

Dr. Carl W. Kumpe, Covington, and Miss Ruth Lang, Cincinnati, Ohio, were married September 14.

Dr. William Lovell Wright, West Liberty, and Miss Eva Sara Murphy, Lexington, were married October 12.

Dr. Louis Flexner Cleary, Lexington, and Miss Cora Leach Kielkopf, Lynchburg, were married October 9.

DEATHS

Dr. Earle J. Brashear, North Pleasureville, aged 65, died November 27 of bleeding peptic ulcer with secondary anemia.

Dr. Albert Butt, Louisville, aged 82, died recently.

Dr. W. W. Hord, Maysville, aged 78, died recently.

Dr. Shelon Cohn, Fulton, aged 62, died February 6.

Dr. Greene L. Johnson, Harrodsburg, aged 56, died December 4 of carcinoma.

Dr. Charles B. Kobert, Danville, aged 60, died December 12 of a heart attack.

Dr. Joseph S. Lehman, Midway, aged 71, died December 13 of ruptured aneurysm.

Dr. Frank Renel Lord, Covington, aged 68, died November 26 of cerebral edema.

Dr. Charles Frederick Voigt, Midway, aged 47, died November 19.

LOUISIANA

Avoyelles Parish Medical Society has elected Dr. H. J. Kaufman, Jr., Cottonport, President; Dr. W. F. Couvillion, Marksville, Vice-President; and Dr. K. A. Roy, Mansura, Secretary-Treasurer.

Bienville Parish Medical Society has elected Dr. S. S. Speer, Ringgold, President; Dr. C. L. Langford, Gibsland, Vice-President; and Dr. V. W. Fletcher, Ringgold, Secretary-Treasurer.

Iberia Parish Medical Society has elected Dr. J. D. Martin, President; Dr. H. M. Flory, Vice-President; and Dr. C. L. Mengis, Secretary-Treasurer, all of New Iberia.

Jackson-Lincoln-Union Parish Medical Society has elected Dr. Ragan Green, President; Dr. S. L. White, Vice-President; and Dr. J. J. Bennett, Secretary-Treasurer, all of Ruston.

Lafayette Parish Medical Society has elected Dr. E. E. Guilbeau, Carencro, President; Dr. L. A. Prejean, Scott, Vice-President; and Dr. Henry Voorhies, Lafayette, Secretary-Treasurer.

Pointe Coupee Parish Medical Society has elected Dr. J. W. Plauche, Morganza, President; Dr. J. M. Mosely, Lakeland, Vice-President; and Dr. R. A. Kelly, New Roads, Secretary-Treasurer.

Continued on page 42

DR. MOODY'S SANITARIUM

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Founder

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Superintendent

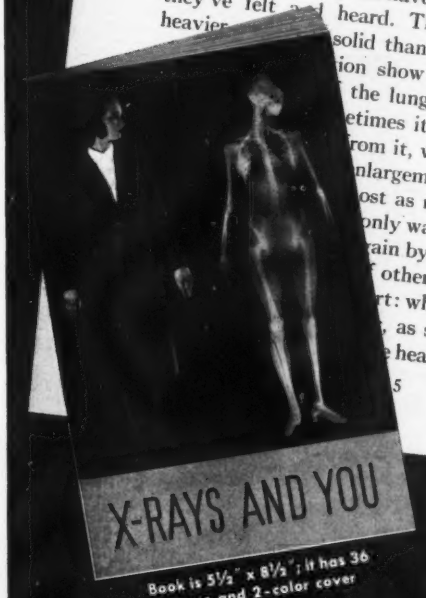
HOW IS YOUR HEART?

THERE are a number of pretty important things in your chest and they all need to be x-rayed from time to time: your ribs, for instance, if there is any chance that you may have broken one; your lungs and bronchial tubes, which we'll be coming to in a minute; and that vital little pump called your heart.

People are apt to think of heart failure as something that comes suddenly like a bolt from the blue. But, as a matter of fact, nobody's heart ever lies down on the job until it has been overworked for years, or has worked under the handicap of millions of visiting and unwelcome germs. And when it does reach the point where it can't go on much longer, it practically always gives warning first ...but you have to heed that warning.

One of the first things the heart does when it is overworked is grow bigger. Doctors can get an idea of this by gently thumping the chest over the heart, and listening, but a lot more certain way is by means of x-ray examination, and they're apt to have one made as a check on what they've felt and heard. The heart

A page from one of the 15 chapters in *X-rays and You*



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Continued from page 40

Tangipahoa Parish Medical Society has elected Dr. J. DeL. Thames, Hammond, President; Dr. R. G. Korniker, Ponchatoula, Vice-President; and Dr. S. J. Cali, Hammond, Secretary-Treasurer.

Webster Parish Medical Society has elected Dr. Rupert Butler, Springhill, President; Dr. R. E. Smith, Minden, Vice-President; and Dr. B. A. Norman, Cotton Valley, Secretary-Treasurer.

Dr. M. Carl Wilensky has been reelected President of the New Orleans Zionist District and Dr. Sidney Jacobs was named Vice-President.

Dr. Gilbert C. Anderson, New Orleans, was elected to membership in the Central Psychiatric Society at a recent meeting in Milwaukee, Wisconsin.

Dr. R. Alec Brown, New Orleans, was reelected Secretary-Treasurer of the Louisiana Association of Public Health Workers at its recent meeting.

Dr. Wm. H. Gillentine, New Orleans, has been appointed State Health Consultant of the National Youth Administration.

Assistant Surgeon Ralph W. Pagel has been relieved of duty at Galveston, Texas, and ordered to proceed to the U. S. Marine Hospital, New Orleans.

Passed Assistant Surgeon Joseph Pasterneck has been relieved at New Orleans and ordered to proceed to the U. S. Marine Hospital, Staten Island, New York.

Dr. E. Z. Browne has been elected President of the Stars and Bars Chapter of Alpha Omega Alpha, national honorary medical fraternity; Dr. W. P. Gardiner, President-Elect; Dr. Joseph N. Ane, Councilor; and Dr. Michael DeBakey, Secretary-Treasurer, all of New Orleans.

New officers of the staff of Mercy Hospital, New Orleans, are: Dr. Theodore F. Kirn, President; Dr. E. J. Richard, Vice-President; Dr. N. J. Tessitore, Secretary; and Dr. Clifford J. Vedrenne, Treasurer.

Dr. Clarence P. May has been appointed to Senior Associate, Department of Neurology, at Touro Infirmary, New Orleans.

Dr. Henry W. E. Walther, New Orleans, has been elected President of the Friends of the Howard-Tilton Memorial Library of Tulane University of Louisiana.

Dr. Julian Graubarth, New Orleans, has been appointed Pediatrician of the City Board of Health to succeed the late Dr. Frank Kinberger.

Dr. James Kirby Howles, Professor of Dermatology and Syphilology and Director of the Department in the School of Medicine of Louisiana State University, has been elected to fellowship in the American College of Surgeons.

Dr. Joseph O. Weilbaecher, Jr., has been appointed Acting Director of Charity Hospital, New Orleans, succeeding Dr. Roy W. Wright, resigned.

Dr. Frank A. Donaldson, Assistant Superintendent of the Mississippi State Hospital, Whitfield, has been named Superintendent of the East Louisiana Hospital for the Insane, Jackson, succeeding Dr. Eugene M. Robards, Jr., who became Acting Superintendent on the recent death of Dr. Charles S. Miller.

Dr. John T. Crebbin, Shreveport, has been elected Superintendent of the Eye, Ear, Nose and Throat Hospital, New Orleans.

Dr. Richard F. Gates, Hammond, was recently named Superintendent of the Floridal Parishes Charity Hospital, Independence.

Dr. Allen L. Cohn, Minden, and Miss Ruby Mae Foster were married October 8.

Dr. James Monteleone Ciaravella, New Orleans, and Miss Frances Anzalone were married recently.

Dr. John Graham Norris, Farmerville, and Miss Mary Inez Taylor were married in October.

Deaths

Dr. William Harrison Floyd, Jena, aged 55, died November 21 of carcinoma of the head of the pancreas.

Dr. Robert Lewis Segrest, Wisner, aged 58, died November 29.

Dr. D. Ross Hinton, Start, aged 53, died November 23 of acute rheumatic fever and influenza.

Dr. George Dewey Sagrera, Arnaudville, aged 40, died November 19 of injuries received in an automobile accident.

Continued on page 44

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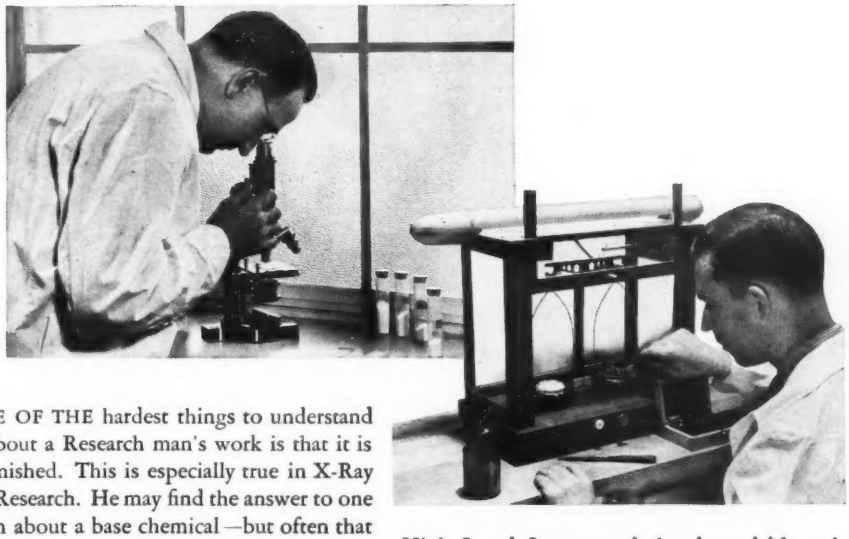

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Continued from page 42

MARYLAND

DEATHS

Dr. Charles Carlin Ayres, White Hall, aged 48, died December 9 of cerebral hemorrhage.

Dr. Hugh Francis Bradley, Jarrettsville, aged 71, died in December of coronary thrombosis, arteriosclerosis and chronic cholecystitis.

Dr. Christian Doetjen, Baltimore, aged 77, died December 28 of arteriosclerosis.

Dr. Lewis F. Hamrick, Baltimore, aged 64, died in November.

Dr. Harry Michael Stein, Baltimore, aged 49, died November 15 of arterial hypertension, nephrosclerosis, diverticulosis of the colon and cholelithiasis.

Dr. William S. Smith, Baltimore, aged 80, died December 9 of uremia.

MISSISSIPPI

Mississippi State Medical Association will hold its next annual meeting in Biloxi, May 13-15.

DeSoto County Medical Society has elected Dr. J. M. Wright, Hernando, President; Dr. A. V. Richmond, Lake Cormorant, Vice-President; and Dr. L. L. Minor, Memphis, Tennessee, Secretary-Treasurer.

Lauderdale County Medical Society has elected Dr. T. G. Cleveland, President; Dr. W. Jeff Anderson, Vice-President; and Dr. R. L. Donald, Secretary-Treasurer, all of Meridian.

South Mississippi Medical Society has elected Dr. H. G. Cook, Hattiesburg, President; Dr. Tom Ramsey, Laurel, First Vice-President; Dr. C. C. Thompson, Jr., Columbia, Second Vice-President; and Dr. J. P. Culpepper, Jr., Hattiesburg, Secretary-Treasurer.

Dr. George E. Gibbons, Shreveport, Louisiana, formerly serving as relief Director of Tallahatchie County Health Department while Dr. E. W. Ryan was away on scholarship, is now Health Officer of the Noxubee County Unit.

Dr. George B. Neukom, New Orleans, has been appointed Director of the Panola County Health Department.

Dr. R. L. Simmons, Meridian, formerly Assistant Health Officer of the Lauderdale County Training Center, is Pearl River County Health Director.

Dr. W. B. May is Assistant Health Officer of the Lauderdale Training Center.

Dr. C. A. Bailey, formerly on the staff of the Rockefeller Foundation, is now Acting Director of the Yazoo County Health Department.

Field Memorial Hospital was formally opened at Centreville on February 28. It is operated by Dr. R. F. and Dr. S. E. Field.

Dr. Augustus Street, Vicksburg, was elected President of the Mississippi Chapter of the American College of Surgeons at the meeting on the coast, January 31, and Dr. T. E. Ross, Hattiesburg, Secretary-Treasurer.

DEATHS

Dr. Charles Dennis Mitchell, Whitfield, aged 74, died January 25.

Dr. Edward James O'Rourke, Cambridge, aged 54, died November 20 of coronary heart disease.

MISSOURI

Caldwell-Livingston Counties Medical Society has elected Dr. Henry H. Patterson, Braymer, President, and Dr. V. D. Vandiver, Chillicothe, Secretary.

Cole County Medical Society has elected Dr. Thomas J. Kelly, President; Dr. Harry B. Stauffer, Vice-President; and Dr. James A. Hill, Secretary-Treasurer, all of Jefferson City.

Grundy-Daviess Counties Medical Society has elected Dr. E. J. Mairs, President; Dr. O. R. Rooks, Vice-President; and Dr. E. A. Duffy, Secretary-Treasurer, all of Trenton.

Henry County Medical Society has elected Dr. J. W. Galbreath, Urich, President, and Dr. Edwin C. Peeler, Clinton, Secretary.

Mercer County Medical Society has elected Dr. G. M. Bristow, Princeton, President, and Dr. J. M. Perry, Princeton, Secretary-Treasurer.

Phelps-Crawford Counties Medical Society has elected Dr. A. H. Horne, Steelville, President; Dr. A. A. Drake, Rolla, Vice-President; and Dr. R. E. Breuer, Newburg, Secretary-Treasurer.

Continued on page 46

PLASTIGUT

A New Universal Suture

truly non-reactive, non-capillary, guaranteed physiologically inert

Increasing numbers of surgeons are unanimous in their approval of Plastigut . . . the first real advance in more than 50 years toward an ideal suture.

Plastigut is a synthetic plastic especially selected to meet suture requirements. It is truly non-reactive, non-capillary and non-absorbable, guaranteed physiologically inert. There is no danger in leaving it in place, as it becomes virtually a part of the supporting structures. After two years it has been found perfectly intact.

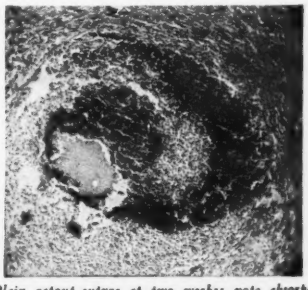
Due to greater tensile strength, Plastigut is used in small sizes, four only being necessary. The 4-0 is recommended for ties and the 00 for all other general work. For plastic surgery 5-0 is recommended. Size 0 is used as a heavy tension suture. Black is provided for skin work in sizes 0, 4-0 and 5-0. Plastigut may be sterilized by autoclaving, without vacuum, for 15 minutes. For office use it may be boiled.

PRICE—Plastigut in envelopes, length 60 inches
(specify size and whether plain or black)

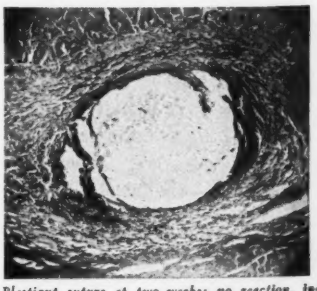
Dozen $2.40
Gross $25.00

A. S. ALOE COMPANY

19th and Olive Streets ST. LOUIS, MISSOURI



Plain catgut suture at two weeks; note absorption and inflammation.



Plastigut suture at two weeks; no reaction, inflammation or absorption.

ORETON-M

in tablets, is the new, *orally effective* androgen producing full male hormone effects *by mouth* — valuable as the supplementary or complete treatment of male sex hormone deficiencies.

ORETON Ampules are standard for male hormone therapy by injection, furnishing intense, prolonged activity for all androgen indications: hypogonadism, the male climacteric, impotence with androgenic deficiency, prostatism, control of functional uterine bleeding, suppression of lactation, after-pains and breast engorgement.

ORETON

ORETON-F

Ointment affords highly effective absorbtion of the male sex hormone when massaged into the skin—a convenient, potent mode of administration. In tubes and in single-dose *Toplicators*.

ORETON-F* FOR *FREE* MALE HORMONE; ORETON,* THE PROPIONATE; ORETON-M,* THE *METHYL* COMPOUND

*Trade-Marks Reg. U. S. Pat. Off.

SCHERING CORPORATION • BLOOMFIELD • NEW JERSEY

. . . only the **BAXTER VACOLITER** *gives you a*

***Visible* PROOF OF VACUUM**

When tamperproof seal is removed, two depressions in rubber diaphragm indicate vacuum is intact, and that parenteral solution in VACOLITER is fresh, pure and uncontaminated.

***ONLY* BAXTER *HAS THE* FILTERDRIP**

A safety feature of the Transfuso Vac technique. This stainless steel mesh of the FILTERDRIP filters *every* drop of blood, preventing clots from passing through tubing.

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Produced and distributed in the Eleven Western States by DON BAXTER, INC., Glendale, Cal.

Distributed East of the Rockies by

AMERICAN HOSPITAL SUPPLY CORP.

CHICAGO NEW YORK

Continued from page 44

Ste. Genevieve County Medical Society has elected Dr. R. C. Lanning, President; Dr. G. M. Rutledge, Vice-President; and Dr. R. W. Lanning, Secretary-Treasurer, all of Ste. Genevieve.

Dr. E. A. Doisy, St. Louis, Director of the Biochemistry Department of the School of Medicine of St. Louis University, has been named a member of the National Advisory Cancer Council.

Dr. Harry Sturgeon Crossen, Professor Emeritus in Gynecology at Washington University School of Medicine, St. Louis, since 1935, was guest of honor at a dinner given at the University on November 23.

DEATHS

Dr. Percy Hypes Swahlen, St. Louis, aged 63, died December 10 of coronary thrombosis.

Dr. Frederick W. Veninga, St. Louis, aged 55, died November 10 of chronic myocarditis.

Dr. James B. Wood, St. Louis, aged 47, died November 23.

NORTH CAROLINA

Medical Society of the State of North Carolina will hold its next annual meeting at Pinehurst, May 19-21.

Dr. Tinsley R. Harrison, a native of Alabama, a graduate of the University of Michigan Medical School and Johns Hopkins University School of Medicine, and formerly Associate Professor of Medicine at Vanderbilt University School of Medicine, Nashville, Tennessee, is the newly appointed Professor of Medicine at the Bowman Gray School of Medicine of Wake Forest, Wake Forest. Dr. Wingate Johnson, Winston-Salem, is Professor of Clinical Medicine; Dr. James P. Rousseau, Winston-Salem, Professor of Radiology; Dr. John A. Rose, Philadelphia, Pennsylvania, Associate Professor of Psychiatry; and Dr. Frank R. Lock, New Orleans, Louisiana, Associate Professor of Obstetrics and Gynecology.

An Evacuation Hospital Unit is being organized from the staff of Memorial Hospital, Charlotte, with Dr. Paul Sanger heading the movement.

Dr. Lonnie N. Little, Statesville, has been elected Health Officer of Iredell County, succeeding Dr. Ross S. McElwee.

Dr. W. H. Patton, Jr., Morganton, has been elected Health Officer of Burke County.

Dr. Spencer Bell, Hamptonville, has been elected Health Officer of Yadkin County.

Dr. Albert A. Kossove and Dr. Irene L. Kossove announce the opening of offices for the general practice of medicine in Charlotte.

Dr. William Edward Adair, Jr., and Miss Lucy Blake Ward, both of Wilmington, were married in October.

Dr. Daniel Smith Currie, Jr., Parkton, and Miss Marion Cox Wood, Vanceboro, were married October 26.

Dr. George Rudolph Laub, New Bern, and Miss Harriet Elizabeth Stith, Columbia, South Carolina, were married in October.

Dr. William McConnell Jones, Gastonia, and Miss Elizabeth Garlington were married October 14.

Dr. William Alexander Graham and Miss Ermine DeGraffenried Peek, both of Durham, were married January 11.

Dr. Hunter McGuire Sweaney and Miss Frances Leake Foushee, both of Durham, were married December 31.

Dr. McLean Bacon Leath, Jr., High Point, and Miss Lillian Boswell Agnew, Inverness, Virginia, were married December 31.

Dr. J. S. Chamblee and Miss Willie Elizabeth Evans, both of Windsor, were married December 28.

Dr. George Benjamin Fleetwood Traylor, Lumberton, and Miss Leslie Chappell Bradshaw, Waverly, Virginia, were married December 21.

Dr. Joseph Spurgeon Hiatt and Miss Sara Elizabeth Rankin, both of Gastonia, were married January 3.

Dr. Thomas Clarkson Worth, Raleigh, and Miss Barbara Donaldson Luther, Oleans, New York, were married January 4. Dr. Worth is now stationed at Fort Benning, Georgia, as a lieutenant in the Medical Corps, U. S. Army.

DEATHS

Dr. Lytle Caldwell Adams, LaGrange, aged 63, died December 8 of heart disease.

Dr. Benjamin Wise Burt, Holly Springs, aged 78, died November 14 of arteriosclerotic heart disease.

Dr. Allan Carruthers Banner, Greensboro, aged 45, died January 11 of a heart attack.

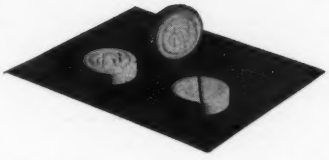
Dr. Silas Asa Conduff, Mount Airy, aged 59, died January 13 of a heart attack.

Continued on page 48

A New Development

ORAL TABLETS

OF MALE SEX HORMONE



NEO-HOMBREOL (M) tablets, methyl testosterone 'Roche-Organon,' now make possible effective oral replacement therapy of male sex hormone deficiency. Three to four 10-mg. Neo-Hombreol (M) tablets by mouth are equivalent to 10 mg. testosterone propionate by injection. The marked oral effectiveness of methyl testosterone, amply demonstrated in experimental and clinical studies alike, vastly increases the convenience of male sex hormone medication. In the words of one investigator, oral administration of methyl testosterone "may ultimately replace all other methods of using testosterone or its propionate." (Foss, *Brit. M. J.*, 1939, 2:11).

Neo-Hombreol (M) tablets may be prescribed in all conditions in which male sex hormone therapy is indicated, such as eunuchism (including cases of castration), hypogonadism (eunuchoidism), and male climacteric symptoms (impotence, etc.) in men, and certain cases of hypermenorrhea, dysmenorrhea, intermittent mastopathia, menopausal disturbances, and for the suppression of lactation in women. Physicians are invited to write for a special descriptive leaflet giving dosage recommendations.

• Neo-Hombreol (M) tablets, 10 mg. methyl testosterone each, are individually wrapped in sanitape and packaged in cartons of 15 and 30. (Note: Methyl testosterone is also highly active by cutaneous absorption. For use by inunction, Neo-Hombreol (M) Dosules are available, each containing 2 Gm. absorbable ointment base incorporating 4 mg. methyl testosterone, in boxes of 25).

NEO-HOMBREOL (M) TABLETS
(Methyl Testosterone)
EFFECTIVE ORAL THERAPY

ROCHE-ORGANON, INC. • NUTLEY • NEW JERSEY

In Canada: ROCHE-ORGANON, LTD. • MONTREAL • TORONTO

Continued from page 46

Dr. Amos Carson Duncan, Forest City, aged 46, died December 10 of mesenteric thrombosis and cirrhosis of the liver.

Dr. Hugh Parks, Elkin, aged 44, died in November of cardiovascular disease and coronary occlusion.

Dr. L. Lester Self, Cherryville, aged 62, died December 4 of myocarditis and coronary thrombosis.

OKLAHOMA

The next annual meeting of the Oklahoma State Medical Association will be held at the Skirvin Tower Hotel, Oklahoma City, May 19-22.

Deaths

Dr. Albert G. Austell, Center, aged 80, died October 28 of heart disease.

Dr. Richard Arthur Byrd, Edmond, aged 58, died November 18.

Dr. Robert Erle Evans, Ada, aged 31, died December 31 of injuries sustained in a highway collision.

Dr. David Middleton Lawson, Nowata, aged 73, died November 23 of diabetes mellitus and chronic myocarditis.

Dr. Ronald Tobertson Smith, Tulsa, aged 56, died in November of heart disease.

SOUTH CAROLINA

South Carolina Medical Association will hold its next annual meeting at the Poinsett Hotel, Greenville, April 15-17.

Charleston County Medical Society will continue Dr. Joseph H. Cannon and Dr. T. E. Bowers for their two-year terms as President and Vice-President, respectively. Dr. Joseph I. Waring and Dr. W. Cyril O'Driscoll were reelected Secretary-Treasurer and Librarian, respectively.

A new National Guard Medical Unit will be organized in Columbia under the command of Captain R. W. Ball.

Dr. J. Y. O'Daniel, who has been Director of the Marlboro County Health Department for five years, has resigned to enter private practice in Ellijay, Georgia.

The Esdorn Hospital, Walterboro, has received a gift of $1,000 from the estate of Franklyn L. Hutton, which will be applied toward additions planned for the hospital.

Dr. Jennings Cleckley recently opened offices at Bamberg for the practice of medicine.

Chicago Eye, Ear, Nose & Throat College
Established 1897
231 W. Washington St., Chicago, Ill.
Practical postgraduate course in Ophthalmology and Otolaryngology.
Doctors admitted at any time for review and clinical observation.
Two residencies of one year each now available.
OSCAR B. NUGENT, M.D., Director

Providence Hospital, Columbia, has elected to its staff: Dr. O. B. Mayer, Chief; Dr. R. B. Durham, Vice-Chief; and Dr. R. B. Josey, Secretary. Dr. Tom Pitts, Dr. F. E. Zemp and Dr. William Weston, Jr., are the Staff Committee.

Dr. Eugene Leroy Horger, Clinical Director of the South Carolina State Hospital, Columbia, was elected to honorary membership in the Phi Beta Kappa fraternity of Wofford College because of his scholarly attainments and his cultural interests since his undergraduate days at Wofford.

Dr. L. B. King, Lake City, has reported to Fort Jackson for active duty in the U. S. Army.

Dr. Paul Eugene Payne and Miss Sybil Lee, both of Columbia, were married January 1.

Dr. Andrew M. Jamison, Jr., Spartanburg, and Miss Evelyn Byrd Hardin were married October 27.

Dr. John H. Robinson, III, Spartanburg, and Miss Betty Watson, Portsmouth, Virginia, were married in November.

Deaths

Dr. John G. Stanley, Marion, aged 65, died January 6 of injuries received when his car collided with a truck.

Dr. William Austin Tripp, Easley, aged 74, died December 21.

Dr. L. W. Wood, Slater, aged 52, died December 28.

Dr. Edmund Waring Simons, Summerville, aged 73, died November 17.

Dr. Manney Rice, Columbia, aged 61, died December 25.

Dr. Benjamin Lucas Norwood, McBee, aged 74, died December 8 of bronchopneumonia and nephritis.

TENNESSEE

Tennessee State Medical Association will hold its next annual meeting at the Noel Hotel, Nashville, April 8-10.

Bradley County Medical Society has elected Dr. William A. Garrott, Cleveland, President; Dr. Madison S. Trewhitt, Cleveland, Vice-President; and Dr. H. H. Hudson, Dyersburg, Secretary-Treasurer.

Davidson County Medical Society has elected Dr. N. S. Shofner, President; Dr. J. P. Gilbert, Vice-President; and Dr. Hamilton V. Gayden, Secretary, all of Nashville.

Knox County Medical Society has elected Dr. Jesse Hill, President; Dr. John R. Smott, Vice-President; and Dr. Robert B. Wood, Secretary-Treasurer, all of Knoxville.

Dr. Gilbert J. Levy announces the removal of his office to the Doctors Building, Memphis.

Dr. Edward C. Ellett, Memphis, was elected a Vice-President of the National Society for the Prevention of Blindness to fill the vacancy left by the recent death of Dr. Francis Park, of Buffalo, New York.

Dr. James D. Biles, Jr., Memphis, and Miss Elizabeth Hough Boone, Seattle, were married September 7.

Dr. John Malcolm Aste and Mrs. Jane Boyce Crump, both of Memphis, were married October 3.

Dr. Arthur Caldwell Dunlap and Miss Emily Jeannette Mandle, both of Paris, were married October 5.

Dr. Claud Walter Perry, Jr., and Miss Marie Katherine Jenkins, both of Chattanooga, were married September 14.

Continued on page 50

LaMOTTE BLOOD CHEMISTRY SERVICE

LaMotte N (1-Naphthyl) Ethylenediamine Dihydrochloride LaMotte Ammonium Sulfamate
For determining Sulfathiazole and related compounds, according to the method of Marshall and Bratton.
These products are prepared and standardized in our research laboratory, and are available in packages of convenient size, for immediate use in these determinations.

This Service includes a series of similar outfits for conducting the following accurate tests: Blood Sugar, Blood Urea, Sulfathiazol, Sulfapyridine and Sulfanilamide in Blood. Icterus Index, Phenolsulphonphthalein Urine pH, Blood pH, Gastric Acidity, Calcium-Phosphorus, Blood Bromides, Blood Proteins, Urinalysis.

LaMOTTE CHEMICAL PRODUCTS CO., Dept. S, Towson, Baltimore, Maryland

THESE STANDARDS *help assure* NORMAL WEIGHT GAIN

TOGETHER

. . . WITH EXCELLENT TISSUE TURGOR AND PROPER BONE STRUCTURE:

1. A suitable fat, easily digested, readily assimilated.
2. A protein that provides the amino acids essential for adequate nutrition and growth.
3. Lactose in correct proportion to protein and fat.
4. 10 mg. Iron and Ammonium Citrate per quart.
5. Vitamins A, B_1 and D in adequate amounts.
6. 20 calories per ounce.

S.M.A.,* when diluted ready to feed, meets these standards.

S.M.A. gives excellent nutritional results—consistently, economically.

Normal infants relish S. M. A. . . . digest it easily and thrive on it.

" " "

*S.M.A., a trade mark of S.M.A. Corporation, for its brand of food especially prepared for infant feeding—derived from tuberculin-tested cow's milk, the fat of which is replaced by animal and vegetable fats, including biologically tested cod liver oil; with the addition of milk sugar and potassium chloride; altogether forming an antirachitic food. When diluted according to directions, it is essentially similar to human milk in percentages of protein, fat, carbohydrates and ash, in chemical constants of the fat and physical properties.

FOR PREMATURE AND UNDERNOURISHED INFANTS
A Special Product

PROTEIN S.M.A.
(Acidulated)

Protein S.M.A. (acidulated) is a modified form of S.M.A., intended to meet the special nutritional needs of the premature and undernourished infant and for infants requiring a high protein intake.

Protein S.M.A. (acidulated) is similar to both casein milk and lactic acid milk, but presents additional nutritional elements lacking in both.

S.M.A. CORPORATION • 8100 McCORMICK BOULEVARD • CHICAGO, ILLINOIS

Continued from page 48

DEATHS

Dr. James Pringle Crawford, Nashville, aged 73, died November 25.

Dr. Frank B. Easley, Chattanooga, aged 39, died December 29.

Dr. C. M. H. Farrar, Hillsboro, aged 92, died November 11 of acute nephritis.

Dr. Harry Quigg Fletcher, Chattanooga, aged 57, died December 7 of pulmonary embolism following coronary occlusion.

Dr. Victor John Ganey, Winchester, aged 26, died November 20.

Dr. John Evans Hanna, Jr., Knoxville, aged 76, died November 26 of chronic cardiorenal disease.

Dr. J. L. Shirley, Chattanooga, aged 82, died November 9.

Dr. L. L. Tilley, Lebanon, aged 71, died December 18.

Dr. David Morgan Woodward, Huntsville, died January 1.

TEXAS

State Medical Association of Texas will hold its next annual meeting in Fort Worth, May 12-15.

The thirteenth Annual Spring Clinical Conference of the Dallas Southern Clinical Society will be held at the Hotel Adolphus, Dallas, March 17-20.

Anderson-Houston-Leon Counties Medical Society has elected Dr. Leroy Trice, Palestine, President; Dr. Paul B. Stokes, Crockett, Vice-President; and Dr. John H. Barrett, Palestine, Secretary-Treasurer.

Collins County Medical Society has elected Dr. W. G. Harris, Plano, President; Dr. W. Scott Wysong, Jr., McKinney, Vice-President; and Dr. H. Dudley Wysong, McKinney, Secretary-Treasurer.

The El Paso County Medical Society has installed Dr. Harry Varner, President, and elected Dr. F. O. Barrett, President-Elect; Dr. C. W. Awe, Vice-President; and Dr. L. W. Breck, Secretary-Treasurer.

Gonzales County Medical Society has elected Dr. N. A. Elder, Nixon, President; Dr. W. A. Sievers, Gonzales, Vice-President; and Dr. George W. Wilhite, Gonzales, Secretary-Treasurer.

Hardin-Tyler Counties Medical Society has elected Dr. Watt Barclay, Woodville, President; Dr. W. J. Pshataske, Silsbee, Vice-President; and Dr. Alvin Waller, Woodville, Secretary.

Harrison County Medical Society has elected Dr. Rogers Coke, President; Dr. J. B. Baldwin, Vice-President; and Dr. F. V. Mondrik, Secretary-Treasurer, all of Marshall.

Henderson County Medical Society has elected Dr. R. E. Henderson, President, reelected; Dr. J. K. Webster, Vice-President; and Dr. Don Price, reelected, all of Athens.

Kaufman County Medical Society has elected Dr. T. S. Howell, Terrell, President; Dr. E. D. Lane, Terrell, Vice-President; and Dr. R. J. Rowe, Jr., Kaufman, Secretary-Treasurer.

Panola County Medical Society has elected Dr. C. F. Hull, Carthage, President; Dr. W. G. Carnathan, Carthage, Vice-President; and Dr. Lynn C. Hooker, Carthage, Secretary-Treasurer.

Tarrant County Medical Society has elected Dr. R. J. White, President-Elect; Dr. Bert C. Ball, Vice-President; and Dr. W. P. Higgins, Secretary-Treasurer, all of Fort Worth.

Wichita County Medical Society has elected Dr. W. J. Masters, President; Dr. F. R. Landon, Vice-President; and Dr. R. L. Nelson, Secretary-Treasurer, all of Wichita Falls.

Baylor Hospital, Dallas, was recently presented by Dr. and Mrs. Stanley J. Seeger, of Milwaukee, Wisconsin, a gift of $10,000 for the establishment of a blood plasma and serum center at the Hospital. The gift was made through the Southwestern Medical Foundation, of which Dr. Edward H. Cary, Dallas, is President, and will be a memorial to Mrs. Seeger's father, the late William Buchanan, of Texarkana. Dr. Seeger is Chairman of the Council on Industrial Health of the American Medical Association.

A new clinic building has been completed at a cost of $35,000 in Beaumont and was built to provide clinical facilities for Dr. John A. Hart, Dr. R. B. Stevens and Dr. J. Fertitta.

Passage of a $285,000 bond issue provides for the erection of a county tuberculosis hospital in San Antonio.

Dr. George W. Cox, Austin, has been reappointed State Health Officer, being the first health officer to be elected for three consecutive two-year terms.

Dr. J. W. Giessel, Eagle Lake, has completed postgraduate work in surgery in the Cook County Hospital, Chicago.

Dr. H. G. Swepston, Rosebud, has been doing postgraduate work at the New York Polyclinic Hospital.

Dr. A. G. Barsh, Stephenville, has been doing postgraduate work at Stanford University, San Francisco.

Dr. E. L. Burton, McKinney, has been doing postgraduate work in New Orleans, Louisiana, and in New York.

Dr. Harold M. Williams, Fort Worth, is Acting Director of the Health and Welfare Department of the City of Fort Worth during the year's absence of Dr. Burke Brewster, who is now stationed at Camp Brownwood.

Dr. Leon Kopecky and Dr. Ina Moody Calhoun, both of San Antonio, were married November 5.

Continued on page 52

Classified Advertisements

RATES for insertion in the Classified Column are as follows: $2.00 minimum, which includes the first 50 words; for each word in addition to the original 50 words, the charge is 3c.

WANTED: Well trained doctor under 40 years of age for general practice and some surgery to become an associate with a busy Oklahoma City general practitioner. Address inquiries to Dept. M-30, care JOURNAL.

REPRESENTATIVE WANTED—Salesman, now calling upon the medical and dental professions, to carry profitable side-line offered by prominent medical publisher. Write fully to A. W. Volland, The C. V. Mosby Company, 3525 Pine Boulevard, St. Louis, Missouri.

WANTED—Experienced man as assistant resident; large traumatic and fracture service; American, Class A school; personal interview; salary commensurate with position; state race, religion and nationality. Address inquiries to Dept. D-12, care SOUTHERN MEDICAL JOURNAL, Birmingham, Alabama.

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THEOPHYLLINE-ETHYLENEDIAMINE

American Made from American Materials

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HEMATINIC PLASTULES*

The Modern Iron Therapy

● Hematinic Plastules provide ferrous iron in small soluble elastic capsules—a modern, convenient dosage form. Where iron therapy is indicated, Hematinic Plastules can usually be relied upon to bring about a steady, rapid rise in hemoglobin. Their administration is seldom complicated by gastric disturbance. . . . Hematinic Plastules are an economical iron preparation especially effective for the treatment of the iron deficiency anemia of pregnancy, for chronic blood loss, or post-infection anemia.

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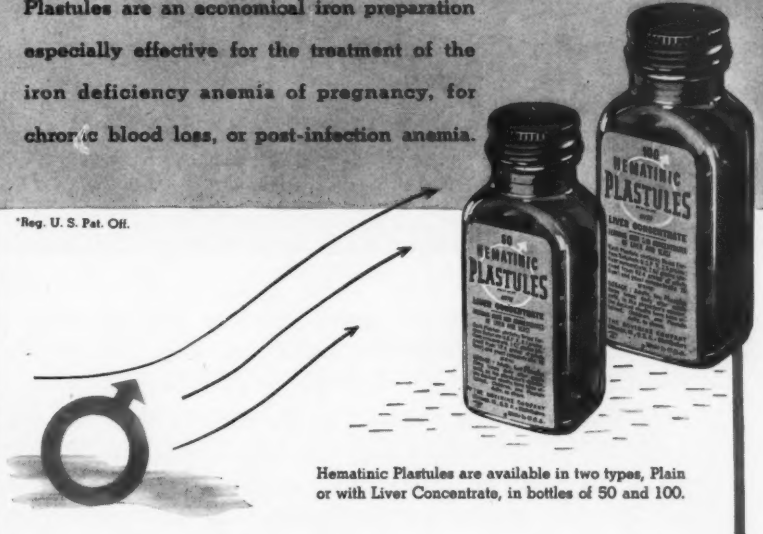

Hematinic Plastules are available in two types, Plain or with Liver Concentrate, in bottles of 50 and 100.

THE BOVININE COMPANY

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Continued from page 50

Dr. Philip Magrish, San Antonio, and Miss Edith Stone were married September 5.

Dr. M. J. Kuykendall, Wortham, and Mrs. Minnie Lloyd, Blooming Grove, were married December 25. They are making their home in Blooming Grove.

Dr. J. W. E. H. Beck has moved from DeKalb to Austin.

Dr. R. B. Burns has moved from Giddings to Midland.

Dr. John A. Crockett has moved from Harlingen to Austin.

Dr. B. H. Estess has moved from Austin to Jasper.

Dr. C. W. Evans, Jr., has moved from Fastrill to El Paso.

Dr. Kenneth R. Flamm has moved from Amarillo to Camp Bowie, Brownwood.

Dr. H. J. Frachtman has moved from Houston to Fort Crockett, Galveston.

Dr. Hugh Fultz has moved from Premont to Falfurrias.

Dr. John C. Galbreath has moved from Alvin to Longleaf, Louisiana.

Dr. James F. Garmany has moved from Mineral Wells to Lubbock.

Dr. F. W. Halpin has moved from Fort Worth to Fort Crockett, Galveston.

Dr. A. A. Hellams has moved from Ferris to San Antonio.

Dr. T. R. Jones has moved from Beaumont to Houston.

Dr. Ernest C. Reed has moved from Legion to Whipple, Arizona.

Dr. Preston R. Sanders has moved from Big Spring to El Paso.

Dr. Van C. Tipton has moved from Austin to Macon, Georgia.

Dr. Everett P. Veatch has moved from Pasadena to Bolahum, Liberia, West Africa.

Dr. Harold A. Wood has moved from San Antonio to Austin.

Dr. R. B. Wolford has moved from Midland to Fort Worth.

Dr. J. Weldon Carter has moved from Palestine to Tyler.

Dr. D. B. Currie has moved from Kerens to Center.

Dr. D. W. Davis has moved from Sanatorium to George West.

Dr. Fred Harrell has moved from Olney to Marfa.

Dr. L. J. Hawker has moved from Fort Worth to San Antonio.

Dr. James R. Martin has moved from Houston to Dallas.

Dr. Harold D. Parks has moved from Dallas to East St. Louis, Illinois.

Dr. H. Leslie Robinson has moved from Austin to San Antonio.

Deaths

Dr. William E. Menefee, Cleburne, aged 83, died November 13.

Dr. John A. Mercer, Chilton, aged 79, died November 17.

Dr. Samuel Lynn Wadley, Palmer, aged 59, died November 4 of pneumonia.

VIRGINIA

Gill Memorial Eye, Ear and Throat Hospital, Roanoke, will hold its fifteenth annual Spring Graduate Course, April 7-12.

The twelfth annual meeting of the postgraduate surgical assembly of the Southeastern Surgical Congress will meet at the John Marshall Hotel, Richmond, March 10-12, under the presidency of Dr. Irvin Abell, of Louisville, Kentucky. Dr. B. T. Beasley, 701 Hurt Building, Atlanta, Georgia, is Secretary-Treasurer.

The American Academy of Pediatrics will hold a meeting of Region 2, the Southern Group, in Richmond, April 24-25.

Albemarle County Medical Society has elected Dr. William H. Wood, Jr., President; Dr. G. S. Fitz-Hugh, Vice-President; and Dr. E. W. Kirby, Secretary-Treasurer, all of Charlottesville.

Arlington County Medical Society has elected Dr. Henry Louis Bastien, Arlington, President; Dr. Robert H. Detwiler, Vice-President; and Dr. J. R. B. Hutchinson, Arlington, Secretary-Treasurer.

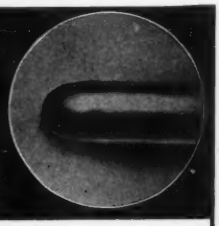
James River Medical Society has elected Dr. A. C. Whitley, Palmyra, President; Dr. E. B. Nuckols, Cumberland, Vice-President; and Dr. Garland Dyches, Secretary-Treasurer, reelected.

Northampton County Medical Society has elected Dr. S. K. Ames, Cape Charles, President; Dr. J. R. Hamilton, Nassawadox, Vice-President; and Dr. W. C. Henderson, Nassawadox, Secretary, reelected.

Dr. G. W. Skaggs, who has been at Dante for three years, has returned to his home in Dublin and resumed practice there.

Continued on page 54

RADON SEEDS



FOR safety and reliability use composite Radon seeds in your cases requiring interstitial radiation. The Composite Radon Seed is the only type of metal Radon Seed having smooth, round, non-cutting ends. In this type of seed, illustrated here highly magnified, Radon is under gas-tight, leak-proof seal. Composite Platinum (or Gold) Radon Seeds and loading-slot instruments for their implantation are available to you exclusively through us. Inquire and order by mail, or preferably by telegraph, reversing charges.

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Continued from page 52

Dr. Henkel M. Price, who has been on the staff of Pine Camp Hospital, Richmond, has located in Martinsville.

Dr. Alex N. Chaffin, formerly of Galax, is now on the medical staff of Catawba Sanatorium.

Dr. J. Dean Creger, of St. Paul, has moved to Radford.

Petersburg Hospital Staff's newly elected officers are: Dr. Meade Edmunds, President; Dr. George Reese, Vice-President; and Dr. Hyman Cantor, Secretary.

Dr. John Warren Montague, Richmond, and Miss May Adelaide Walton, Morganton, North Carolina, were married January 4.

Dr. Edward Stewart Orgain, Richmond, and Miss Ann Foreman Lewis, Durham, North Carolina, were married December 28.

Dr. Albert Joseph Orlosky, Arlington, and Miss Nancy Elise Conley, Washington, D. C., were married in October.

Dr. Bathurst B. Bagby, West Point, former Director of the Bureau of Child Health in the State Health Department, has been appointed temporarily Epidemiologist and Chief Health Officer of Richmond, succeeding Dr. William A. Brown, resigned. Dr. Brown is Health Officer of Alexandria.

Dr. Walter J. Rein, recent associate in ophthalmology of the late Dr. Emory Hill, announces the continuation of his practice at the same address, Professional Building, Richmond.

Deaths

Dr. Paul Brandon Barringer, Charlottesville, aged 84, died January 9.

Dr. Prentiss Dupuy Johnston, Tazewell, aged 62, died January 3, following a paralytic stroke.

Dr. Francis Lee Thurman, Buena Vista, aged 74, died January 19.

Dr. Franklin Pierce, Norfolk, aged 86, died January 18.

WEST VIRGINIA

West Virginia State Medical Association will hold its next annual meeting at Charleston, May 12-14.

Barbour-Randolph-Tucker Counties Medical Society has elected Dr. L. U. Lumpkin, Elkins, President; Dr. L. S. King, Philippi, and Dr. J. M. Brand, Coketon, Vice-Presidents; and Dr. Guy H. Michael, Belington, Secretary-Treasurer, reelected.

Boone County Medical Society has elected Dr. A. E. Glover, Madison, President; Dr. D. E. Lewis, Nellis, Vice-President; and Dr. H. H. Howell, Madison, Secretary-Treasurer.

Greenbrier County Medical Society has elected Dr. Herbert Duncan, Lewisburg, President; Dr. E. W. McCauley, Rainelle, Vice-President; and Dr. A. G. Lanham, Secretary-Treasurer, reelected.

Harrison County Medical Society has elected Dr. Richard V. Lynch, Meadowbrook, President; Dr. J. T. Brennan, Clarksburg, Vice-President; Dr. R. T. Humphries, Clarksburg, Treasurer; and Dr. L. E. Neal, Clarksburg, Secretary.

Marion County Medical Society has elected Dr. Kyle Y. Swisher, Fairview, President; Dr. Philip Johnson, Fairmont, Vice-President; Dr. James L. Blanton, Fairmont, Treasurer; and Dr. John P. Helmick, Fairmont, Secretary, reelected.

Mercer County Medical Society has elected Dr. L. J. Pace, Princeton, President; Dr. J. R. Shanklin, Bluefield, Vice-President; Dr. Frank J. Holroyd, Princeton, Secretary; and Dr. H. G. Steele, Bluefield, Treasurer.

Parkersburg Academy of Medicine has elected Dr. Welch England, Parkersburg, President; Dr. A. R. Lutz, Parkersburg, Vice-President; and Dr. A. C. Woofter, Parkersburg, Secretary-Treasurer.

Preston County Medical Society has elected Dr. J. F. Lehman, Kingwood, President; Dr. H. C. Miller, Eglon, Vice-President; and Dr. C. Y. Moser, Kingwood, Secretary-Treasurer, reelected.

Wetzel County Medical Society has elected Dr. B. F. Matheny, Hundred, President; and Dr. R. F. Miller, Paden City, Secretary-Treasurer.

Dr. William W. Davis, Parkersburg, and Miss Mary Lydenberg were married October 5.

Dr. Homer Jackson Hancock, Welch, and Miss Harriet Loyd Hudgins, Warrenton, North Carolina, were married October 26.

Deaths

Dr. Frank Theodore Dare, Wellsburg, aged 64, died January 21 of carcinoma.

Dr. Russell Arthur Salton, Williamson, aged 53, died January 20.

Dr. Fleming Howell, Buckhannon, aged 91, died January 9.

Dr. Oliver H. Griffith, Wheeling, aged 53, died January 15.

Dr. Joseph A. Wood, Pratt, aged 83, died January 9.

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1930

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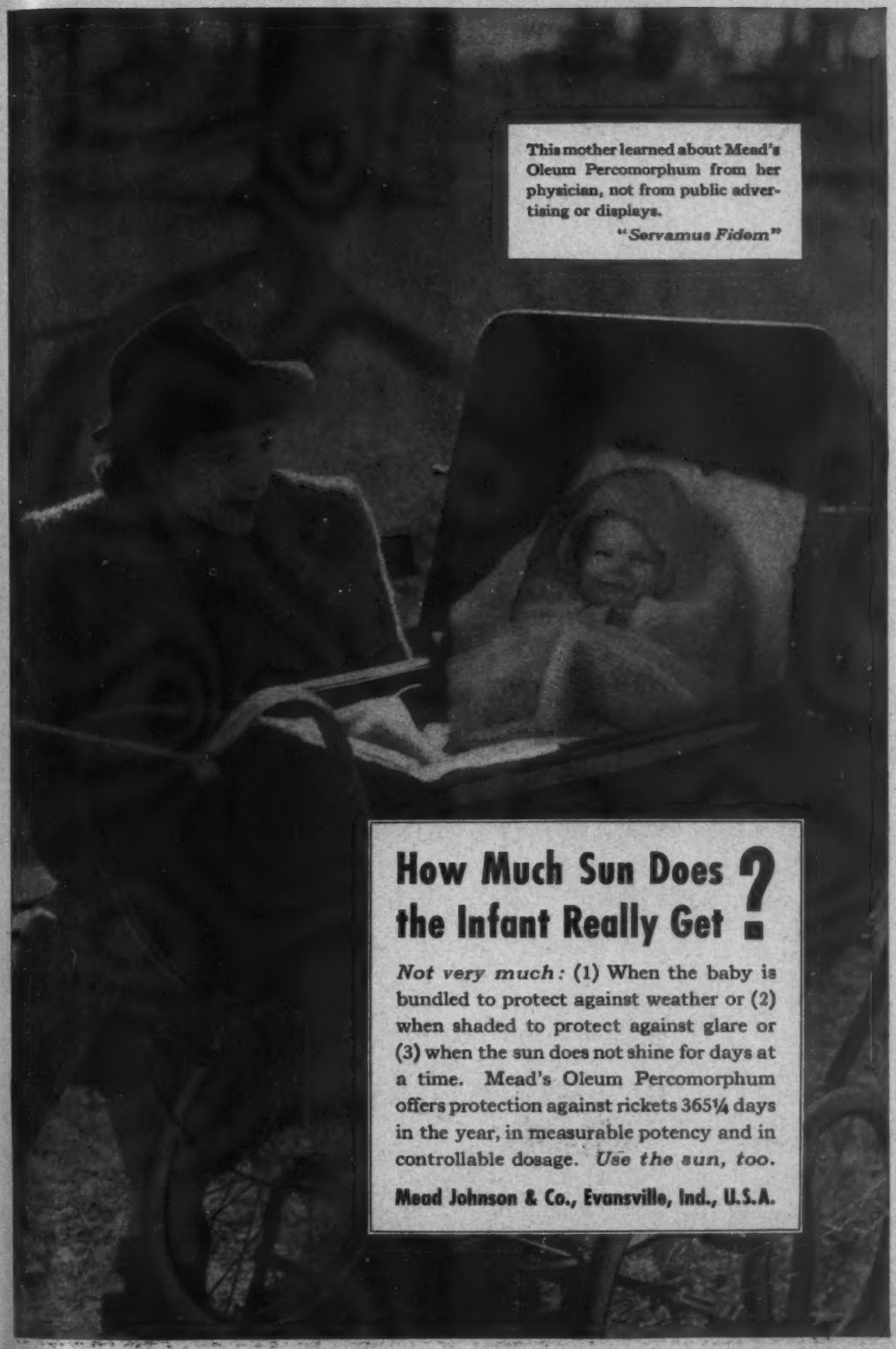
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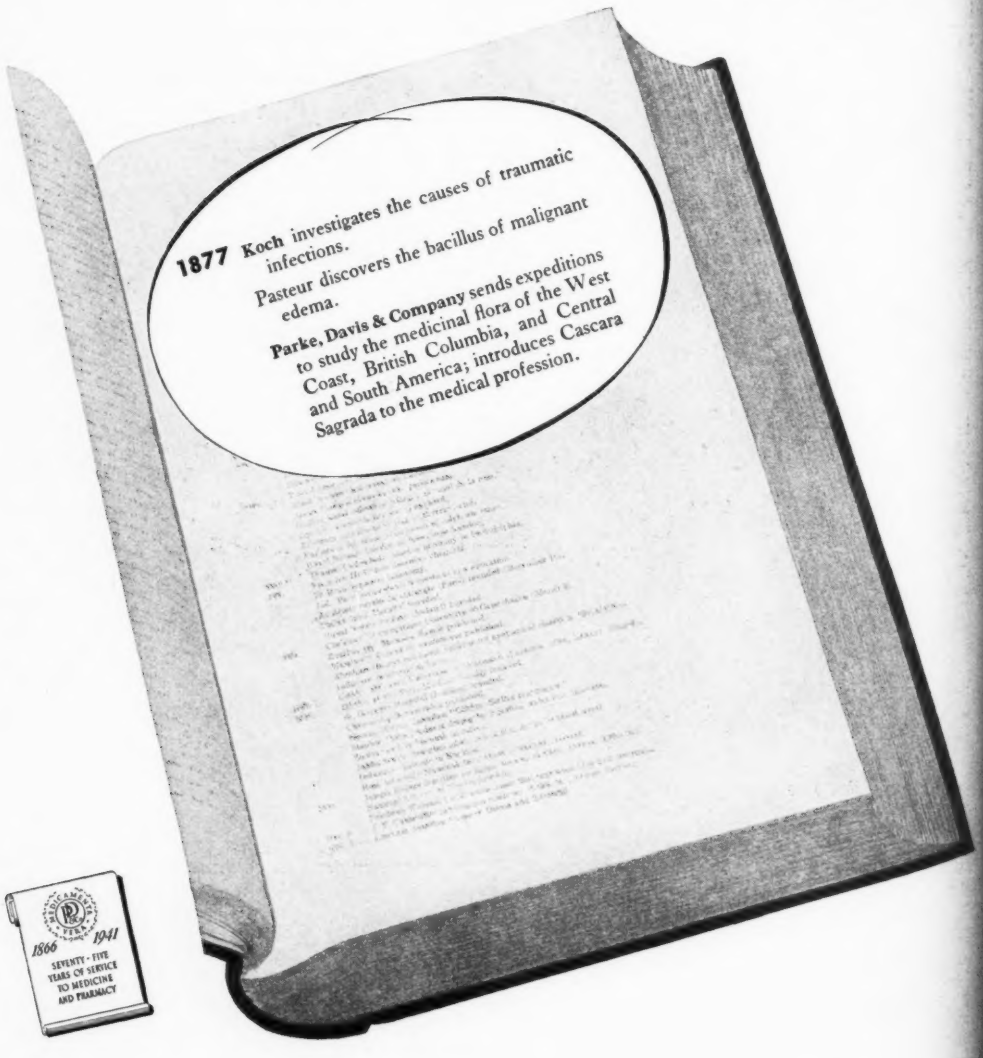
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